Impact of short course

Prophylactic antibiotics

In poisoning

A randomized double blind placebo controlled trial

A dissertation submitted in partial fulfillment of the degree of **MD Branch-I (General Medicine)** examination of the Tamil Nadu **Dr. MGR Medical University, Chennai**

CERTIFICATE

This is to certify that the work presented in this dissertation, in partial fulfillment of the degree of **MD Branch-I (General Medicine)** examination of the Tamil Nadu **Dr. MGR Medical University, Chennai** entitled **"Impact of short course prophylactic antibiotics in poisoning"** is a bonafide work of Dr**. John Jose. E**, post graduate student in **MD(General Medicine).** It was carried out and prepared under my overall guidance and supervision in the department of Medicine, **Christian Medical College Hospital, Vellore.**

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ABSTRACT

TIitle: Impact of short course prophylactic antibiotics in poisoning. A randomized double blind placebo controlled trial.

Objective: The primary objective of the study was to evaluate the impact of a short course prophylactic antibiotics for the prevention of pneumonia in patients aged fourteen years and above who receive gastric lavage for poisoning.

Design: Single centre, prospective, randomized double blind placebo controlled trial

Setting: A 2200 bedded tertiary care teaching hospital in South India.

Participants and methods: A randomized double blind placebo controlled trial was performed aiming at the reduction of the incidence of pneumonia in poisoned subjects. Between October 31st 2005 and August 1st 2006, one hundred and four patients who were hospitalized following poison ingestion and received gastric lavage were included in the study. Of the 104 subjects, 53 were randomized into the prophylactic antibiotic group (a combination of three doses of crystalline penicillin 20 lakh units given four hours apart and single dose of Levofloxacin 500 mg administered intravenously) and 51 into the placebo group. Primary outcome was the occurrence of pneumonia as defined by the objective criteria. Secondary outcome measures were mortality, duration of intensive care and hospital stay and of mechanical ventilation.

Results: Overall 12 patients fulfilled the objective criteria for pneumonia. Nine were in the placebo group and three in the prophylactic antibiotic group. (p= 0.056). The risk ratio for patients receiving prophylactic antibiotics compared to patients receiving

placebo was 0.32 [95% confidence interval, CI=0.09 -1.12]. Although the risk reduction in terms of aspiration pneumonia with antibiotics was 68%; this did not reach statistical significance. All pneumonia occurred in the mechanical ventilated population. Out of 32 ventilated patients, 12 developed pneumonia, 3 in the antibiotic group and 9 in the placebo group.(p value= 0.014).The risk ratio for patients receiving patients receiving prophylactic antibiotics compared to patients receiving placebo in the was 0.29 [95% confidence interval, CI = 0.10 - 0.89]. Number needed to treat to avoid an episode of pneumonia was 2.3 in the mechanical ventilated population. No differences in the other outcome parameters were found.

Conclusions: Use of short course antibiotic prophylaxis of a combination regimen of three doses of intravenously administered crystalline penicillin and a single dose of levofloxacin showed a trend towards a reduction in the incidence of pneumonia in poisoned patients randomized to the prophylactic antibiotic group. A subgroup analysis of mechanical ventilated patients revealed that prophylaxis is probably an effective strategy for the prevention of pneumonia in mechanically ventilated poisoned subjects. These observations justify the conduct of a larger prospective study to evaluate the role of prophylactic antibiotics in poisoned patients.

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Introduction

Poisoning remains a major health problem despite regulatory intervention and medical advances. Worldwide, more than three million poisoning cases with a quarter million deaths occur annually, of which, 99% of fatal poisonings occur in developing countries.[1] In recent times, several advances have been made in the discipline of clinical toxicity that have significantly improved the treatment modalities and methods for poison treatment. However deaths due to poisoning are on a constant rise particularly in developing countries where poisoning is associated with a high case fatality rate.[2,3] Several factors contribute to the high mortality rate in poisoning; one of the important causes being respiratory failure complicating aspiration pneumonia.[4,5,6]

Aspiration is a common event in poisoned subjects and carries with it the risk of development of aspiration pneumonitis and pneumonia. Pneumonia rates in poisoned subjects vary from 4 to 50%.[7,8,9] Several risk factors contribute to the development of aspiration pneumonia and gastric decontamination is one among them.[8,9] Aspiration pneumonia results in substantial morbidity and mortality and leads to increased use of antibiotics, mechanical ventilation, prolonged hospital stay and increased costs of treatment.[9-11]

Any intervention that can reduce the incidence of aspiration pneumonia and the morbidity and mortality associated with it is worthy of study. One such intervention would be the use of prophylactic antibiotics to reduce the development of pneumonia. However there exists a difference of opinion among physicians on the role of prophylactic antibiotics. Clinicians in developing countries often prefer to start antibiotics in poisoned subjects[12] considering the severity of the poisoning and the magnitude of the morbidity imposed by aspiration pneumonia. However this practice is not evidence based. In fact, to the best of our knowledge, there has been no randomized controlled trial that has evaluated the impact of prophylactic antibiotics in the setting of poisoning. Short course systemic prophylactic antibiotics in other clinical settings[13,14] have been shown to reduce the risk of pneumonia and associated morbidity. Hence we decided to conduct a randomized controlled trial to evaluate the impact of a short course prophylactic antibiotic regimen for prevention of pneumonia in the setting of poisoning.

Hypothesis

Hypothesis for the study was as follows.

Would the administration of a short course of systemic antibiotic prophylaxis (three doses of crystalline penicillin 20 lakh units at four hourly intervals and single dose of Levofloxacin 500 mg intravenously administered) reduce the incidence of pneumonia in adult patients presenting with poisoning and receive gastric lavage.

Review of the literature

Poison and poisoning have been known since time immemorial. The use of poison dates back to the earliest humans, who used animal venoms and plant extracts for hunting, warfare and assassination. The Ebers papyrus (circa 1500 B.C) contains information pertaining to many recognized poisons including hemlock (the state poison of the Greeks), aconite (a Chinese arrow poison), opium and metals such as lead, copper and antimony. There are several references to poisons and their use as means of suicide or as a weapon for homicide in the literature of ancient Greece.[15,16]

Poison may be defined as a substance which when administered, inhaled or swallowed is capable of acting deleteriously on the body.[15,16] Probably one of the best known definitions of poison is that by Paracelsus[15,16] [more properly known as Theophrastus Phillippus Aureolus Bombastus von Hohenheim], alchemical genius of the middle ages and father of modern toxicology. Paracelsus over 400 years ago had stated, “All substances are poisons; there is none which is not a poison. The right dose differentiates a poison and a remedy.”

In recent times, owing to the vast developments made in the field of chemical technology, a significant number of new compounds used in the field of trade, industry and medicine have been added as poisonous substances. Poisoning with such compounds either accidental or suicidal has become common due to easy availability and low cost. Increasing

mortality and morbidity associated with poisoning is a growing concern among medical fraternity of the developing world. The case fatality for self-poisoning in the developing world is commonly 10–20%, but for particular pesticides it may be as high as 50–70%. [3]

The causes of the high case fatality are multifactorial but include the high toxicity of locally available poisons, difficulties in transporting patients across long distances to hospital, the paucity of health care workers compared with the large numbers of patients, and the lack of facilities, antidotes, and training for the management of pesticide-poisoned patients.[3,16] The problem is compounded by a lack of proven interventions with which to develop treatment protocols. Complications such as seizures, arrhythmias, hypotension, respiratory failure and pneumonias compound the problem and contribute to the increased mortality. As mentioned earlier, aspiration pneumonia in poisoned subjects is associated with an increased use of antibiotics, antimicrobial resistance, super infections, prolonged hospital stay and increased costs of treatment. It has been shown previously that drug overdose is a common cause of aspiration, ranging from 29% to 50 % of patients in studies conducted in intensive care units. [9,18-19] Identification of the predisposing risk factors and strategies such as prophylactic antibiotics may help lessen the burden of pneumonia.

Epidemiology

GLOBAL BURDEN OF POISONING

Poisoning is an important health problem worldwide, though the type of poison and the associated morbidity and mortality may vary from place to place and change over a period of time. According to WHO more than three million cases of poisoning occur worldwide annually, of which, 99% of fatal poisonings occur in developing countries particularly among agricultural workers.[1] In developed nations like the United Kingdom, about 15-20% of the workload of medical units and emergency departments are due to self poisoning. [20,21] Acute poisoning is an important medical emergency and major cause of morbidity and mortality in developing countries like India. It is reported that 1 to 1.5 million cases of poisoning occur every year in India. [22] Poisoning imposes a health burden which differs from many other common conditions affecting public health. Apart from 68.2 hospitalizations per year per 100,000 populations[23] and subsequent hospital stay and costs, poisoning has significant impact on the after effects in the patients' and caregivers' lives. These effects may be reflected not only in the mental and the physical health of the victim but also in the legal, social and occupational health of the society at large.

PROFILE OF POISONING

A detailed knowledge about the nature and magnitude of the poisoning cases in a particular area is not only important for early diagnosis and prompt treatment but also is essential for introducing new and evaluating old treatment measures. In developing countries deliberate self harm account for most cases of poisoning (Figure1).[3,24,25] Recent adverse life events, interpersonal stress and relationship difficulties, severe financial distress, unemployment, mental illness, chronic illness, use of alcohol, lack of religious faith etc are the major risk factors reported for deliberate self harm.

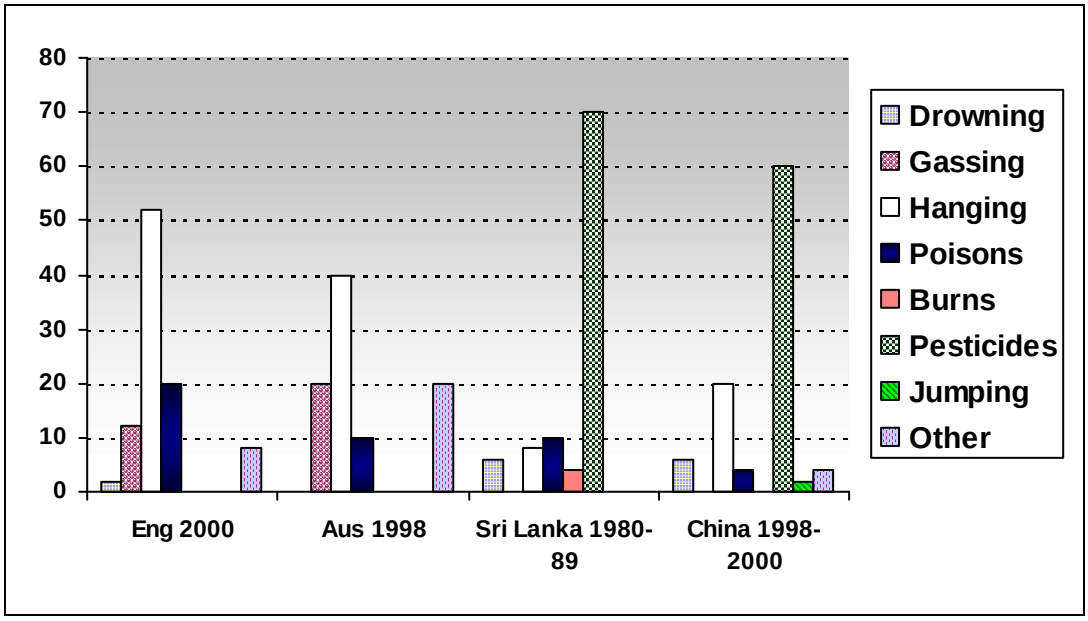

Figure.1. Comparison of methods used for fatal self harm in England & Wales, Australia, and Asia. [3, 24,25]

Tablet overdose is the most common cause of poisoning in the developed world. In the United Kingdom, paracetamol remains the most common drug taken in overdose (50% of intentional self poisoning presentations).[26,27] In developing countries[3] like India and Sri Lanka, majority of the poisoning are due to organophosphate insecticides used for agricultural purposes. This is mainly because of their wide usage and easy availability. In India several profile studies on poisoning have been conducted and in most series poisoning was intentional with a male preponderance. Insecticides such as organophosphates were the most common compounds involved in poisoning. Profile of poisoning in different parts of the country[28-31] is summarized in the table below (table.1). In the Christian Medical College and Hospital, Vellore organophosphate poisoning accounts for 12% of all medical intensive care unit admissions and 75% of all poisonings. [34]

MORTALITY

Everyday around the world, almost 700 people die from poisonings and for every person that dies, several thousands more are affected by poisoning.[1,35] In developed nations like the United Kingdom, nearly 4000 deaths occur per year due to poisoning.[21] In India nearly 50,000 die annually due to poisoning.[35]

Region	No of patients	Males (%)	Intenti-onal (%)	Common Poisons involved	Mortality (%)
Delhi 1999-2002 Srivastava et al[28]	2719	57	53	Household- 44.1% Drugs- 18.8% Pesticides- 12.8% (aluminium phosphide most common)	Not available [N.A]
Rohtak 1994 Siwach SB et al[29]	559	66	91.4	Aluminium Phosphide-67.8% Organophosphates-13.9% Zinc phosphide- 4.3%	33.82% Aluminium phosphide-67.6%
Mangalore 2001-2003 Singh et al[30]	33207	70	72	Agrochemical -49 Drugs-17% Alcohols-13%	15% Organophosphate-65% Aluminium phosphide-15%
Mangalore 1999-2003 Unnikrishnan et al[31]	546	69.6	68	Organophosphates-35.7% Alcohols-12.4% Drugs-11.8%	Not available [N.A]
Yavatamal Maharashtra 1997-2001[32]	4245	67	63.4	Organophosphate-23.1% Alcohol-21% Organochlorine-12%	28.5% Organophosphate-43.3%
Thomas et al Christian medical college, Vellore[33]	1584	M:F 5:4	90.6%	Organophosphate-49.4% Drugs-22.5% Household chemicals-10.2% Plant poisons-5.6%	3.3% Organophosphate-38.4%

Table. 1. Pattern of poisoning in India

Case fatality rate for poisoning varies among the different parts of the world. For every 1000 self poisoning patients admitted to European hospitals, fewer than five die[36.] For every 1000 admitted to rural Asian

hospitals, 100-200 die.[3] Organophosphate compounds were responsible for the majority of deaths in most series of self poisoning cases in rural

areas of the developing world. The reported fatality in hospital based surveys[3] was as high as 46%. Mortality rate for poisoning deaths in various studies conducted in India is reported between 3.3% and 34%.[29,33] Mortality in poisoning depends on the severity of poisoning; mechanisms of toxicity and other complications such as aspiration pneumonia. Mechanisms of toxicity and mortality rate of common poisonings encountered in the Christian Medical College Hospital (CMCH), Vellore are illustrated in the figure below (figure.2). A more recent report from CMCH[37] showed a mortality of around 14% in organophosphate poisoned patients admitted to the medical intensive care unit.

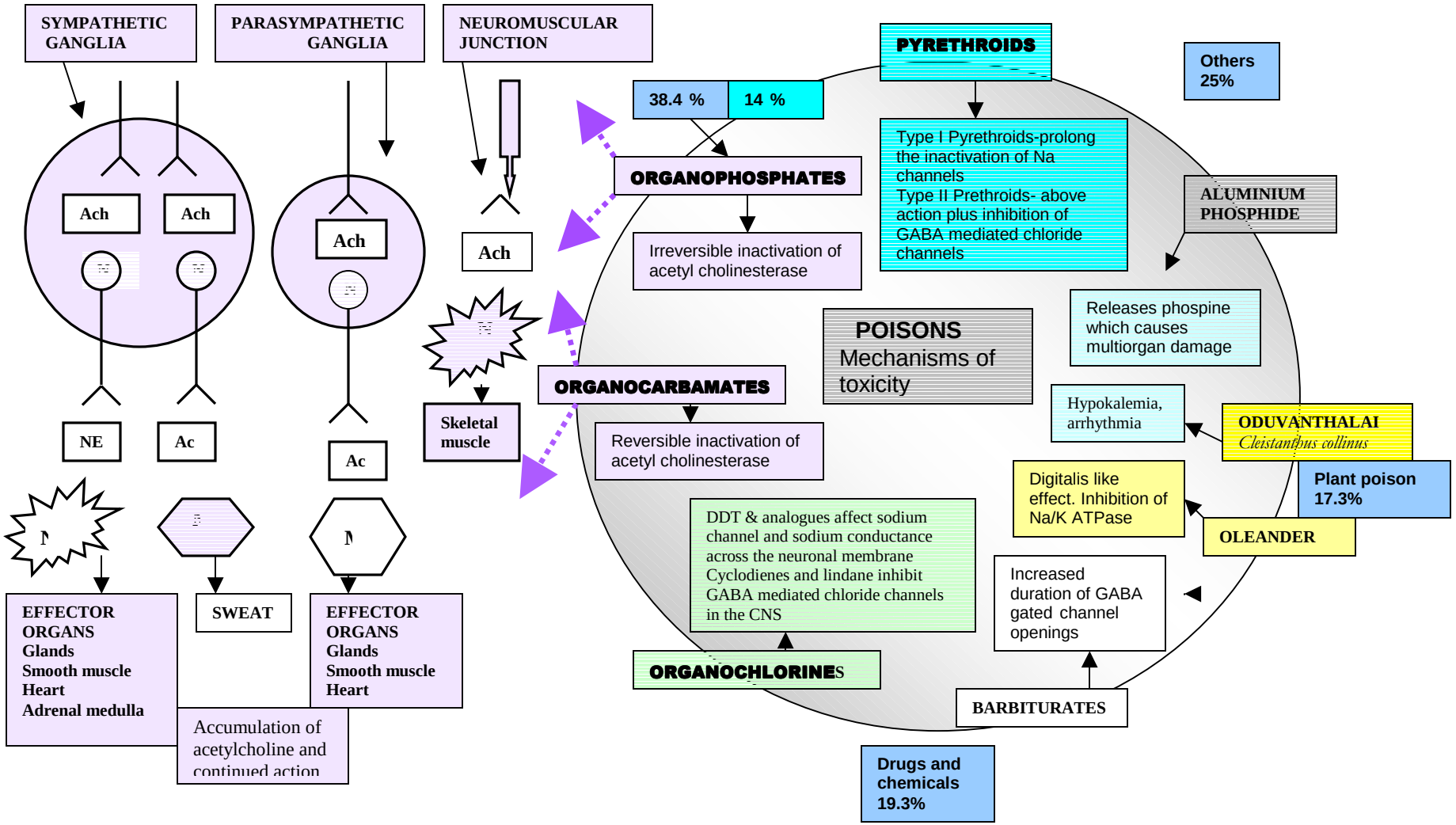

Figure. 2. Mechanisms of toxicity of common poisons encountered in Christian Medical college and Hospital [cmch] Vellore. Mortality rates in CMCH[33,34] for common poisons are given in the boxes

[Kindly ignore this page and view the page below]

Pneumonia in poisoning

In recent times, several advances have been made in the field of toxicology which has increased our knowledge of the chemistry of poisons, modes of toxic action and detoxification processes as well as specific molecular events in the poisoning process. All these advances have revolutionized the fundamentals of poisoning care (figure 3). However the mortality and morbidity associated with acute poisoning, especially in developing countries, remains high.

There are many different direct causes of death in poisoning- hypotension, paralysis, respiratory failure, arrhythmia, electrolyte imbalance etc. Among them, respiratory failure[4,5] is considered to be the one of the most important causes of morbidity and mortality in acute poisoning especially with compounds such as organophosphates; the commonest poison ingested in this region. Respiratory failure has been shown to correlate with mortality in several studies. Patients with poisoning may have respiratory failure for many reasons, including aspiration of gastric contents, excessive secretions, pneumonia, sepsis and adult respiratory distress syndrome. Aspiration pneumonia is an important cause for respiratory failure with consequences of increased use of antibiotics, prolonged duration of mechanical ventilation and hospital stay, and increased costs of treatment.[10]

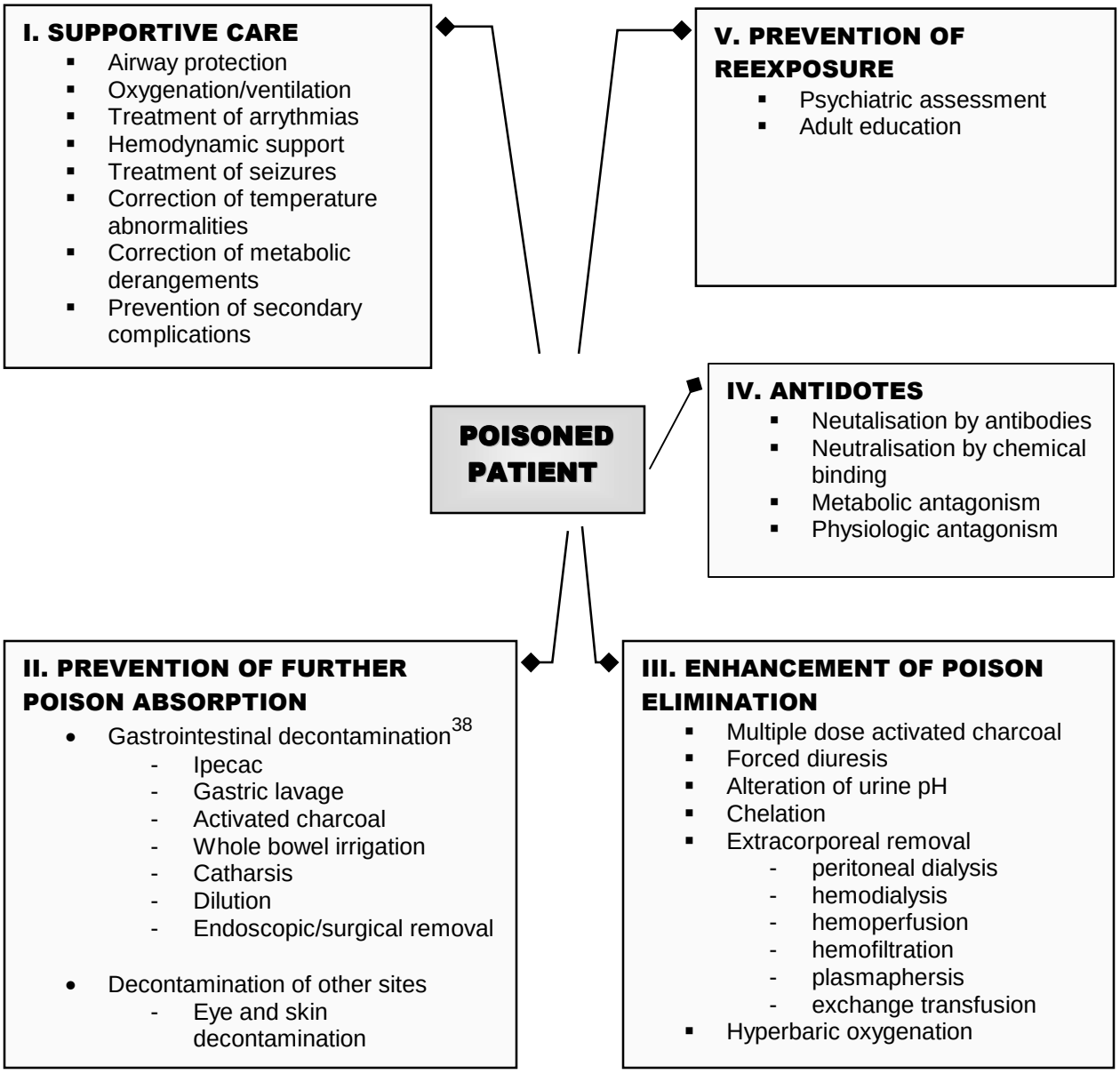

Figure.3. Fundamentals of Poisoning Management[38]

Aspiration pneumonitis versus aspiration pneumonia

Aspiration can be divided broadly into two distinct entities with overlapping features -- aspiration pneumonia and aspiration pneumonitis. Aspiration pneumonitis is a chemical injury to the lung parenchyma by the acid contents of the stomach. [27] In contrast, aspiration pneumonia differs in being a bacterial infection resulting from oropharyngeal flora being aspirated. Bacterial colonization and sepsis are common sequelae in aspiration pneumonia. However bacterial colonization and sepsis may also occur in severe aspiration pneumonitis. This is because resulting lung inflammation can contribute to a subsequent infection, since the material aspirated may contain anaerobic or other unusual causes of pneumonia. Experimental studies provide adequate data for this.

Experimental studies[40,41] have shown that the severity of acute lung injury is related not only to the volume and acidity of the aspirate but also to its composition. Knight et al[40] compared the inflammatory potential of small gastric particles to acidic lung injury and examined their interaction. Results of their experimental study showed that the aspiration of gastric contents (i.e, acidified food particles) lead to inflammatory changes in lung with capillary leak, release of inflammatory cytokines and chemokines, cellular infiltration, surfactant dysfunction, hypoxemia and oxidative injury of greater magnitude than those resulting from the aspiration of acid or gastric particles alone. Although the acidity of the

stomach generally prevents the growth of bacteria, aspiration of nonsterile gastric contents can lead to the development of pneumonia. This occurs, for instance, in patients receiving antacids who aspirate pathogenic organisms colonizing the less acidic stomach or more commonly, following concomitant aspiration of the oropharyngeal flora. The above data is summarized in the figure below (figure. 4)

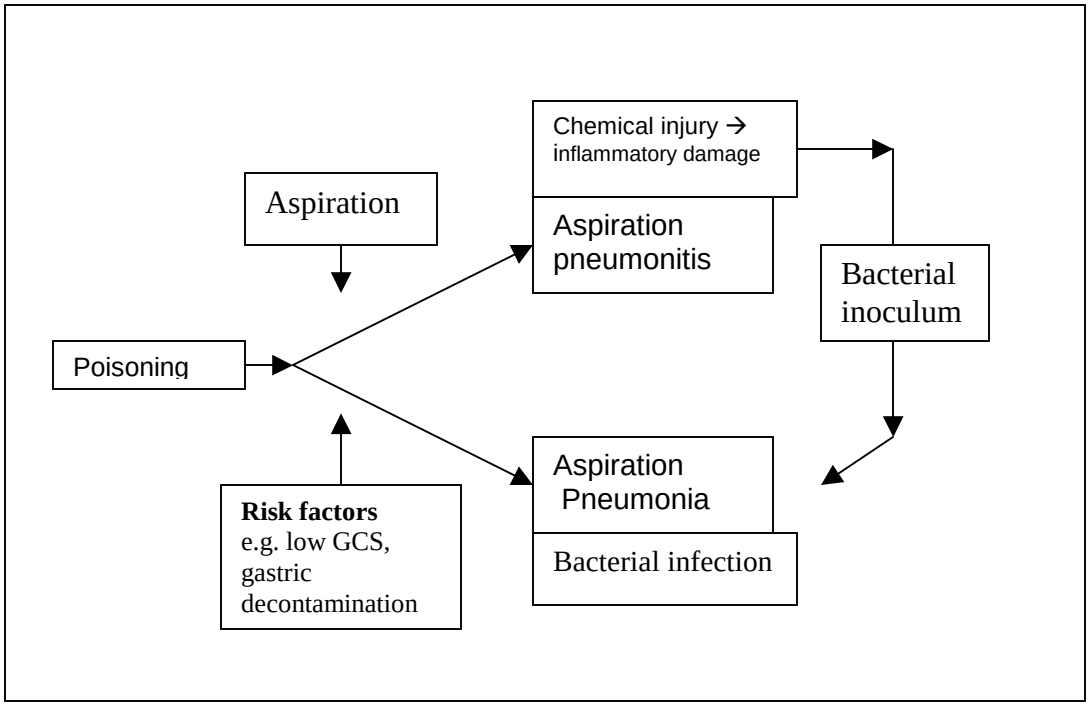

Figure. 4. Schematic representation of events that may occur following aspiration.

Subsequent studies have shown that aspiration insult primes the host to an exuberant inflammatory response when confronted with an ensuing infectious challenge; and the resulting inflammatory milieu and injury adversely influences the host's ability to clear bacteria. Rotta et al[42]

established an animal model of secondary bacterial pneumonia following gastric aspiration and described possible mechanisms involved in the suppressed antibacterial defenses following the initial pulmonary insult. In this controlled in vivo laboratory study gastric aspirate (1.2 mL/kg of saline, pH 1.25, and 40 mg/ml sterile rat gastric particles) or an equal amount of normal saline (pH 5.3) was instilled intratracheally into study animals. One minute after this insult, animals received an intratracheal instillation of either 5.6×10^5 colony-forming units of Escherichia coli or an equal volume of normal saline. Animals that received gastric aspirate (followed by normal saline or E. coli) had increased injury as assessed by significant reductions in oxygenation and elevations in bronchoalveolar lavage albumin. At 24 hours, animals that received gastric aspirate inoculation followed by E. coli had significantly higher pulmonary bacterial counts compared with animals that received E. coli alone. Gastric aspiration injury followed by bacterial inoculation also resulted in acute, but transient, increases in tumor necrosis factor-alpha, interleukin-1 beta, cytokine-induced neutrophil chemoattractant-1, and macrophage inflammatory protein-2 and more sustained elevations of monocyte chemoattractant protein-1 and interleukin-10. These results suggest that following gastric aspiration lung injury increases and bacterial clearance decreases. Similar pulmonary inflammatory milieu is likely to occur following aspiration in a poisoned subject with consequent risk for bacterial pneumonia.

Pneumonia incidence and Diagnosis

There exists a wide variation in the reported rates of pneumonia following poisoning in different studies which probably reflect the differences in the type of poison ingested, severity of poisoning, level of consciousness and various other factors. The reported incidence varies from 4% to 50% in different studies.[4-6,8,9,17-19,43-46] An audit of 204 patients admitted to our institution following poisoning over a period of 10 months during 2004-2005 revealed 35% incidence of pneumonia within four days of hospitalization (unpublished local epidemiological data)

There are no specific diagnostic tests for aspiration pneumonia. The diagnosis in most settings is usually based on new findings of hypoxemia, pulmonary infiltrates in gravity dependant lung regions, fever, and leucocytosis. Microbiological diagnosis is often difficult because of the problems in obtaining specimens of deep respiratory tract without contamination by oral flora and the often limited laboratory capacity for isolation of anaerobic organisms.

Several authors[4,8,19,47,48] have used a constellation of clinical findings for the diagnosis of pneumonia. The criteria for aspiration for most authors were modifications of those defined by Lorber and Swenson[49] and Bartlett et al[50]: namely, the presence of alveolar infiltrates on the chest radiograph and either witnessed aspiration or risk factors for aspiration. Clinical criteria used in various studies are tabularized below.

Tsao et al[4]	new pulmonary infiltrates not explained by any other means and with at least two of the following: (1) raised white blood cell count; (2) purulent bronchial secretions; and (3) positive Gram stain and culture
El-Solh et al[47]	(1) the development of new radiographic infiltrate compatible with pneumonia; (*2*) the presence of symptoms or signs suggestive of lower respiratory tract infection (one major criteria of either cough, sputum production, or fever above 38℃ or below 35.5℃, plus two minor criteria of pleuritic chest pain, dyspnea, delirium, increased alveolar arterial gradient, or white blood cell count > 12,000/mm^3, and/or left shift or leukopenia < 3,000/mm^3) necessitating mechanical ventilation; and (*3*) the presence of risk factors for oropharyngeal aspiration
Terpenning et al[48]	Fever>99.5 F, WBC showing a rise of 5000 cells/mm,opinion of attending physician that pneumonia was present, auscultatory findings, characteristic symptoms, sputum production, dyspnoea, chest pain
Marick et al[19]	the presence of alveolar infiltrates on the chest radiograph and either witnessed aspiration or risk factors for aspiration
Liisanantti et al[8]	the presence of new infiltrates on chest radiography associated with leucocytosis and fever or purulent tracheal secretions within 48 h after admission to the hospital.

Table.2 Clinical criteria for aspiration pneumonia in various studies

Clinical criteria for the diagnosis of pneumonia in our study was modified from the above criterion and included

Two or more serial chest radiographs with at least *one* of the following:

- New or progressive *and* persistent infiltrate
- Consolidation
- Cavitation

And, at least *one* of the following:

- Fever (> 38℃ or >100.4℉) with no other recognize d cause
- Leukopenia (<4,000WBC/mm3) *or* leukocytosis (>12,000 WBC/mm3)

- More than 10% of band forms

And at least *two* of the following:

• New onset of purulent sputum, or change in character of sputum, or increased respiratory secretions, or increased suctioning requirements

• New onset or worsening cough, or dyspnea, or tachypnea

• Rales or bronchial breath sounds

• Worsening gas exchange (e.g., oxygen desaturations [e.g., PaO2/FiO2 < 240], increased oxygen requirements, or increased ventilation demand)

OR a modified clinical pulmonary infection score more than 6.[51]

It is often difficult to differentiate pneumonia due to poisoning and decontamination from other forms of pneumonia resulting from aspiration such as the early onset ventilator associated pneumonia, as the findings often overlap. Ventilator associated pneumonia is defined as pneumonia occurring after 48 hours after intubation.[52] However a subset of patients may have pneumonia occurring within the first four days of intubation, known as the early onset pneumonia.[52] Difficulty in differentiation is also compounded by the fact that aspiration pneumonia due to lavage may present after 48 hours of exposure. For the purpose of this study, all pneumonias occurring within four days were assumed to be due to aspiration occurring at the time of decontamination.

Mortality in aspiration pneumonia

Mortality in aspiration pneumonia in various setting varies from 21%-62%.[53,54] Factors associated with death from aspiration pneumonia in a study were: altered mental status, endotracheal intubation, tachycardia, and hypoxemia. [55]

Risk factors for aspiration pneumonia and aspiration pneumonitis in poisoned patients

Risk factors for pneumonia and pneumonitis are numerous and include age, sex, place of admission (ward, intensive care unit, etc), severity of underlying disease, emesis, gastric lavage, activated charcoal, level of consciousness, airway instrumentation (intubation, reintubation, etc) and type of poison. Identification of the risk factors may allow the early identification of these patients for appropriate observation and management. Summary of risk factors for pneumonia and pneumonitis in studies with high incidence of pneumonia is tabulated below.[8,56-60]

A retrospective study conducted by J. Liisanantti et al[8] analyzed 257 patients admitted with severe self-poisoning over a period of eleven years in the intensive care unit of University Hospital, Oulu, Finland. 28.4% of 257 patients fulfilled the clinical criteria of aspiration pneumonia in the study. The risk factors for development of aspiration pneumonia in this study included the use of gastric lavage or activated charcoal in the case of a non-intubated unconscious patient. [Odds ratios of 2.7

(confidence interval, CI 0.8-9.3) and 3.7 (CI 1.01-12.5), respectively] and delay in intubation.

	Host factors	Intervention factors
Liisantti et al[8]		use of gastric lavage or activated charcoal in a non-intubated unconscious patient [odds ratios of 2.7 (confidence interval, CI 0.8-9.3) and 3.7 (CI 1.01-12.5)] delay in intubation
Isbister GK et al[56]	Older age Glasgow coma scle,GCS < 15 (odds ratio, OR 3.14; 95% CI 1.87-5.27), Emesis (OR, 4.17; 95% CI, 2.44-7.13), Seizures Ingestion of tricyclic antidepressants Delayed presentation to hospital (delay of >24 hrs [OR, 4.42; 95% CI, 2.42-8.10]).	
Christ et al[57]	Low GCS Ingestion of opiates Elevated white blood cell counts	
Vucinic et al[58]	Sex Chronic alcohol intake Underlying illnesses Coma	Central venous catheter Vasopressor H2 receptor blocker Corticosteroids
Adnet et al[59,60]	Low GCS Prone body position at the time of discovery	
Merigian et al[10]		Gastric lavage

Table.3. Risk factors for aspiration and aspiration pneumonitis in various studies

Two of the common methods for gastro intestinal decontamination are gastric lavage and activated charcoal. Gastric lavage[39] involves the placement of a wide bore (36-40 French) orogastric tube followed by instilling and then removal of several liters of water in aliquots to wash out the stomach contents.

Gastric lavage is fraught with potential complications[39] which include pneumonia, laryngospasm, hypoxia, hypercapnia, fluid and electrolyte imbalance; and mechanical injury to, or perforation of throat, esophagus and stomach. However the most common complication of lavage is aspiration pneumonia. In some patients this may be due to performing the procedure in comatose patients with an unprotected airway.

Liisantti et al[8] examined retrospectively the medical records of 257 patients with self-poisoning, and calculated an odds ratio of 2.7 (CI 0.8–9.3) for the development of aspiration pneumonitis when gastric lavage was performed in unconscious non-intubated patients.

Merigian et al[10] prospectively studied the effect of gastric emptying and activated charcoal upon clinical outcome in acutely self-poisoned patients. Results of the study showed gastric lavage to be associated with a higher prevalence of aspiration pneumonia (P=.0001) and medical intensive care unit admissions (P =0.0001).

Some authors, however, have found a lower incidence of pneumonia after decontamination. Moll et al[7] found administration of activated charcoal to intubated overdose patients to be associated with a low incidence of aspiration pneumonia

Microbiology of Aspiration pneumonia

There is conflicting information about the range of organisms responsible for aspiration pneumonia. The role of anaerobic organisms from the mouth seemed to be established in the 1970s and 80s using transtracheal and pleural aspiration to obtain specimens from the lower respiratory tract, avoiding the problem of contamination of expectorated sputum by normal mouth flora.

Most patients with aspiration pneumonia have infection with multiple organisms.[49-50]Anaerobic organisms were found to be the predominant pathogens, isolated alone or with aerobes.[49,50,62] More recent studies[18,19] have reported a lower frequency of anaerobic organisms as causative pathogens in aspiration pneumonia. However, these studies did not use comparable sampling methods or detailed anaerobic culture methods. The anaerobic pathogens most frequently isolated in patients with aspiration pneumonia include *Bacteroides, Peptostreptococcus, peptococcus* and *Fusobacterium* species. Streptococcus pneumoniae, Staphylococcus aureus, Hemophilus influenzae, and Enterobacteriaceae

predominated in patients with a community-acquired aspiration syndrome, whereas gram-negative organisms, including *P. aeruginosa,* predominated in patients with a hospital-acquired aspiration syndrome in a recent study.[19]

Identifying organism(s) responsible for pneumonia is often attempted but not achieved in clinical practice for a number of reasons. These include contamination of sputum specimens with oropharyngeal flora, previous treatment with antibiotics and the difficulties using invasive techniques (such as bronchoscopy, transtracheal and transthoracic aspiration) that are more reliable at isolating pathogens. Anaerobic pathogens are difficult to identify even with good laboratory expertise.

Treatment of aspiration pneumonia

The choice of antibiotics should depend on the setting in which the aspiration occurs. Recommended antibiotic regimens[62] for community-acquired aspiration pneumonia include penicillin, clindamycin, beta-lactam and beta-lactamase inhibitor combinations such as ampicillin sodium and sulbactam sodium or penicillin plus metronidazole. Monotherapy with metronidazole has been associated with a high clinical failure rate despite good in vitro activity against most anaerobes. The newer fluoroquinolones (eg, levofloxacin, gatifloxacin, moxifloxacin) have reasonable anaerobic activity and achieve high concentrations in lung tissue and endobronchial secretions. Trimethoprim-sulfamethoxazole and aminoglycosides have little or no activity against anaerobes. A recent[11]

review recommended the use of antibiotic agents with activity against gram-negative organisms, such as third-generation cephalosporins, fluoroquinolones, and piperacillin in addition to the gram positive and anaerobic coverage. Corticosteroids have not been found to be useful in the management of aspiration pneumonitis and pneumonia.[62]

EMPIRICAL ANTIBIOTICS RECOMMENDED FOR THE MOST COMMON ASPIRATION SYNDROMES.

SYNDROME AND CLINICAL SITUATION	ANTIBIOTIC (USUAL DOSE)*
Aspiration pneumonitis	
Signs or symptoms lasting >48 hr	Levofloxacin (500 mg/day)† or ceftriaxone (1–2 g/day)
Small-bowel obstruction or use of antacids or antisecretory agents	Levofloxacin (500 mg/day)† or ceftriaxone (1–2 g/day) or ciprofloxacin (400 mg every 12 hr) or piperacillin–tazobactam (3.375 g every 6 hr) or ceftazidime (2 g every 8 hr)
Aspiration pneumonia	
Community-acquired pneumonia	Levofloxacin (500 mg/day)† or ceftriaxone (1–2 g/day)
Residence in a long-term care facility	Levofloxacin (500 mg/day)† or piperacillin–tazobactam (3.375 g every 6 hr) or ceftazidime (2 g every 8 hr)
Severe periodontal disease, putrid sputum, or alcoholism	Piperacillin–tazobactam (3.375 g every 6 hr) or imipenem (500 mg every 8 hr to 1 g every 6 hr) or a combination of two drugs: levofloxacin (500 mg/day)† or ciprofloxacin (400 mg every 12 hr) or ceftriaxone (1–2 g/day) plus clindamycin (600 mg every 8 hr) or metronidazole (500 mg every 8 hr)

*The doses listed are those for patients with normal renal function.

†Levofloxacin is given by slow infusion over a 60-minute period. Levofloxacin (500 mg/day) may be replaced by gatifloxacin (400 mg/day).

Table.4. EMPIRICAL ANTIBIOTICS RECOMMENDED FOR THE MOST COMMON ASPIRATION SYNDROMES[11]

Antibiotic prophylaxis- Basis

Antibiotic prophylaxis are often indicated in patients who have no evidence of infection but who have been or are expected to be exposed to bacterial pathogens under circumstances that constitute a major risk of infection. The basic principles of antibiotic prophylaxis are as follows. 1.The risk or potential severity of infection should be greater than the risk of side effects. 2. Prophylaxis should be given for the shortest period necessary to target infections. 3. Antibiotics should be given before the expected period of risk or as soon as possible after contact (post exposure prophylaxis). Examples of antimicrobial prophylaxis being infective endocarditis prophylaxis, mupirocin prophylaxis for recurrent staphylococci infections, prophylaxis for cystitis, recurrent cellulitis with lymphoedema, traveler's diarrhea, neutropenic patients, spontaneous bacterial peritonitis, contacts of patients with meningococcal meningitis and various other surgical settings.

From the above discussions, it would be clear that poisoning is common and the magnitude of the problem imposed by aspiration in poisoning is often severe enough to warrant a preventive approach. Many authors do not recommend prophylactic antibiotics in the setting of poisoning. However the recommendations are not evidence based. In fact, to the best of our knowledge, there has been no randomized controlled trial that has evaluated the impact of prophylactic antibiotics in

the setting of poisoning. Short course systemic prophylactic antibiotics in other clinical settings[13,14] of aspiration have been shown to reduce the risk of pneumonia and associated morbidity.

In a recent randomized controlled trial[13] done in comatose patients admitted to an intensive care unit with head injury and stroke, use of short course of prophylactic antibiotic showed reduction in the risk of pneumonia, hospital and intensive care unit stay. In the same clinical trial protective effect against pneumonia was also observed in control subjects who had previously received prophylactic antibiotics.

Effect of short course prophylactic antibiotics on the incidence of early onset pneumonia in critically ill comatose patients were studied in a single centre prospective open study.[14] A three day prophylaxis with ampicillin –sulbactam [3gm every 6 hours for three days] significantly reduced the occurrence of early onset pneumonia in critically ill comatose mechanically ventilated patients

In another randomized placebo controlled double blinded clinical trial[63] in critically ill patients, short course prophylactic antibiotic reduced the incidence of four most common ICU infections including pneumonias.

Is an ounce of prevention worth a pound of cure? The answer depends on how effective, toxic, and costly the ounce of prevention is

relative to the pound of cure. Prophylactic antibiotics have been found to be effective in various settings described above. The other side of the coin is the fact that antibiotic prophylaxis has the potential for serious adverse effects. Rates of antibiotic resistance are increasing in all hospitals.[64] The prevalence of antibiotic resistance in any population is related to the proportion of the population that receives antibiotics and also to the total antibiotic exposure.[65] Prolonged use of broad spectrum antibiotics merely alter the normal flora and may lead to increasing frequency of antibiotic resistance among subsequent hospital acquired infections. Use of prophylactic antibiotics has also risks of side effects. The most significant adverse event associated with penicillin, one of the agents used in this study, is hypersensitivity reactions which can range from a troublesome rash to a life threatening anaphylactic reactions. One-to-ten per cent of patients report a penicillin allergy although many of these will not be confirmed if subjected to the appropriate test.[66] More importantly, the chance of a penicillin reaction following administration of the drug is in the range of 0.7-5 %.[67] An additional problem with the use of prolonged antibiotics is the dramatic increase in the number of cases of colitis caused by *Clostridium difficile*.[68] The prevalence of *C. difficile* infection is related to total antibiotic usage.[68] Use of short course antibiotics may have a lower impact on the emergence of bacterial resistance and problem of antibiotic induced colitis.

There is no literature on the dose and duration of antibiotic prophylaxis in this group of patients (i.e. poisoned subjects who receive gastric lavage). Due to this paucity of data, we decided to choose a short course prophylaxis regimen which was akin to infective endocarditis regimen. We chose penicillin because it was cheap, widely available and offers protection against gram positive organisms as well as anaerobes. Postulate in using additional doses of penicillin was that it would eliminate the incubating bacteria and afford anaerobic coverage. Levofloxacin is one of the agents recommended recently for treatment of aspiration pneumonia[11] and was chosen to provide additional gram negative coverage since gram negative bacteria are being increasingly found in aspiration syndromes. Use of Levofloxacin alone would not have given sufficient anaerobic cover.

In summary, poisoning appears to be a major health problem with significant morbidity and mortality. Pneumonia in poisoned subjects adds to the morbidity and mortality. Measures to prevent pneumonia may be beneficial. Short course systemic prophylactic antibiotics in other clinical settings[13,14] have been shown to reduce the risk of pneumonia and associated morbidity. Hence we endeavored to conduct a randomized controlled trial to evaluate the impact of a short course prophylactic antibiotic regimen for prevention of pneumonia in the setting of poisoning.

AIMS AND OBJECTIVES

The study was undertaken with the following objectives.

PRIMARY OBJECTIVE:

- To evaluate the impact of a short course systemic antibiotic prophylaxis for the prevention of pneumonia in poisoned patients aged fourteen years and above who receive gastric lavage.

SECONDARY OBJECTIVES:

- To assess the impact of a systemic antibiotic prophylaxis on mortality, duration of intensive care unit and hospital stay and of mechanical ventilation in poisoned patients aged fourteen years and above who receive gastric lavage.

PARTICIPANTS AND METHODS

Study design

The study was a **prospective randomized double blind placebo controlled trial** over a period of 9 months between October 31st 2005 and August 1st 2006. The study was conducted in the emergency ward, the medical wards and the medical intensive care unit of a tertiary teaching hospital in India (Christian Medical College and Hospital, Vellore). All patients aged fourteen years of age and above presenting to the emergency department following ingestion of a poison and received gastric lavage were eligible for recruitment in the study. Eligible patients were screened for the inclusion and exclusion criteria.

The study was performed in accordance with the Declaration of Helsinki and subsequent amendments and under the regulations of Good Clinical Practice. The study was approved by the Research committee as well as the Ethics committee of the Christian Medical College and Hospital, Vellore (Annexure I). Written informed consent was obtained from close relatives of all subjects before participation in the trial (Annexure II).

Setting

Christian Medical College Hospital is a 2200 bedded tertiary care teaching hospital in South India. The Medical ICU is an 11 bedded facility where

patients from all three medicine units and Medicine related super specialty are admitted.

Inclusion criteria

All patients aged 14 years or older who presents to the emergency department following poison ingestion and receive gastric lavage.

Exclusion criteria

The study excluded subjects who met the following criteria.

- Known hypersensitivity to Beta-lactam antibiotics.
- Any evidence of pulmonary infection at the time of recruitment as suggested by clinical criteria below.
- Any subject who is receiving antibiotics for any other established infection at the time of recruitment.
- Any subject who has received treatment with any antibiotic within the past 4 days
- Pregnant women.
- Patients who had gastric lavage and activated charcoal elsewhere prior to admission were also excluded.
- Patients who ingested non toxic doses of drugs and hence expected to be discharged within 24 hours of admission.
- Refusal by the next of kin to participate in the clinical trial.

Intervention

Recruited patients were randomly allocated to receive prophylactic antibiotics or an identical placebo. Interventions given at the time of recruitment are described below. Randomization was done by Biostatistics department. Simple randomization using random tables was the method used. The randomization codes were conveyed to the pharmacy unit in a sealed envelope. The study drugs and corresponding placebos were visibly indistinguishable and were prepared by independent pharmacists of the Clinical Pharmacology department of the Christian Medical College Hospital, Vellore. They were labeled with an identification number, which was noted in the patients' chart as well as the data abstraction sheet to allow for unblinding after completion of the study. Drugs/ placebo were then handed over to the emergency unit nurses who remained blinded to the trial. Primary investigator assessed the patient for eligibility criteria and the allocation was concealed.

Antibiotic prophylaxis group : Patients randomized to the antibiotic group received a combination regimen of three doses of crystalline penicillin intravenously at a strength and dose of 20 lakh units given every four hours *plus*

Single dose of intravenously administered Levofloxacin 500 mg

Control group*:* These subjects did not receive any prophylactic antibiotics. They received identical appearing intravenous placebo

There is no literature on the dose and duration of antibiotic prophylaxis in this group of patients(i.e poisoned subjects who receive gastric lavage) This prophylactic regimen was considered akin to infective endocarditis regimen and hence short duration of treatment was determined. Prior to randomization, eligible subjects also received a test dose of crystalline penicillin and those who tested positive were excluded from the trial.

All study medications were given immediately after randomization and after chest radiographs and baseline blood samples were taken. In addition all patients received additional supportive therapy and antidotes wherever indicated.

All deaths and adverse effects were monitored by a data monitoring committee. The pharmacy and the data monitoring committee were allowed to break the code in the event of a serious adverse event attributed to the study drug **or** a serious infection for which this knowledge was deemed essential to guide antibacterial therapy. Unblinding was not offered routinely in the event of a respiratory infection.

Data and specimen collection

All data were noted on standardized documentation sheets and exclusively collected by the primary investigator (AnnexureIII). The primary investigator was not involved in patient care or in diagnostic or therapeutic decisions. Data recorded on admission included demographic

and diagnostic information on the patients, interventions, calculations of APACHE II scores. The patients were monitored daily for the presence of pulmonary infections, organ failures and other complications according to the specified definitions. On enrollment, chest radiographs, blood counts and blood chemistries were taken by personnel blinded to the study. Blood counts and chest radiographs were repeated every 48 hours. Additional samples and radiographs were collected if considered necessary by the treating physician. Whenever there was a suspicion of infection, samples were obtained for microbiologic cultures, including endotracheal aspirate and at least two separate blood specimens.

END POINTS

Primary outcome was the occurrence of pneumonia as defined by objective criteria. Objective criterion for pneumonia was defined according to the criteria given by other investigators[4,8,19,47] and based on the CDC criteria for pneumonia.[69]

Two or more serial chest radiographs with at least *one* of the following:

- New or progressive *and* persistent infiltrate
- Consolidation
- Cavitation

And, at least *one* of the following:

- Fever (> 38℃ or >100.4℉) with no other recognize d cause
- Leukopenia (< 4,000 WBC/mm3) *or* leukocytosis (>12,000 WBC/mm3)

- More than 10% of band forms

And at least *two* of the following:

• New onset of **purulent sputum**, or change in character of sputum, or increased respiratory secretions, or increased suctioning requirements

• New onset or worsening cough, or dyspnea, or tachypnea

• Rales or bronchial breath sounds

• Worsening gas exchange (e.g., oxygen desaturations [e.g., PaO2/FiO2 < 240], increased oxygen requirements, or increased ventilation demand)

OR a clinical pulmonary infection score more than 6. (Annexure IV)

Purulent sputum is defined as secretions from the lungs, bronchi, or trachea that contain >25 neutrophils and <10 squamous epithelial cells per low power field (x100).

Change in character of sputum refers to the color, consistency, odor, and quantity.

For the purpose of study, pneumonia occurring within 4 days of hospitalization was assumed to be due to aspiration occurring at the time of decontamination. Pneumonia occurring after four days of intubation was labeled as late onset ventilator associated pneumonia.

Secondary outcomes

Secondary outcome measures were mortality duration of hospital stay, medical intensive care unit stay and mechanical ventilation.

Ethical Issues

1. There is clinical equipoise in this area with no studies reporting a benefit with treatment.

2. Only a short course of antibiotics used to minimize antibiotic resistance as the optimal dose and duration of prophylaxis were not known due to paucity of data in the literature.

3. Project was submitted to the ethics committee of Christian Medical College and Hospital, Vellore and approval was obtained (Annexure I).

4. Informed consent was obtained for all patients in the study from next of kin after explaining the details of the trial.

Sample size calculation and Power

The study was designed to test the hypothesis that prophylactic antibiotics given intravenously would reduce the incidence of pneumonia in the population mentioned above. An audit of the previous ten months data on 204 poisoned subjects showed a pneumonia incidence of about 35% in poisoning subjects. This audit was necessary as there was a wide

variation in the incidence of pneumonia reported in poisoned subjects (4 to 50%.in various studies).[7,8,9]

Assuming an incidence of pneumonia of 35% in the control group, a sample size of 51 in each arm was calculated to be necessary to show a 25% reduction in the incidence of pneumonia in the antibiotic treated group assuming 5% level of significance [alpha = 0.05] and a power [1-beta] of 80%, by two sided test.

Stastical analysis

Stata 8 was used for sample size calculations and power analysis. SPSS version 11 and EPIinfo 2002 were used for the statistical analysis. The continuous variables were expressed as mean $\pm$ standard deviation and categorical variables were expressed as counts (percentages) unless stated otherwise. The endpoints were predefined and analyzed on an intention to treat basis. Continuous variables were analyzed using independent t test when the distribution of the variables were normal and by Mann-Whitney U test when the distribution was not normal. Chi-square and Fisher's exact test were used wherever appropriate for analysis of categorical variables. The risk ratios and the number needed to treat were also calculated wherever appropriate.

RESULTS

I. BASELINE CHARACTERISTICS

Between October 31st 2005 and August 1st 2006, a total of 209 patients were admitted to the hospital with a diagnosis of poisoning / overdose. Hundred and four patients who fulfilled criteria for inclusion were enrolled into the study (figure 5). Of the 104 patients, 53 were randomized to the antibiotic group and the remaining 51 to the placebo group. The reasons for exclusions are summarized in the chart (figure 5). The commonest reason for exclusion was non toxic doses of drug overdoses. No patients were lost to follow up. The baseline characteristics of the study population were found to be comparable and are shown in tables 5-7.

	Prophylactic antibiotic group N=53	**Placebo group N=51**	**p value**
Age mean + SD (yrs.)	28 ± 6	31 ±15	0.843
Males [%]	34 [64.2]	25 [49]	0.119
Diabetes	2 [3.8]	2 [3.9]	1.00
Hypertension	3 [5.7]	0	0.243
Smoking habit	10 [18.9]	7 [13.7]	0.478
Alcohol intake	15 [28.3]	7 [13.7]	0.069
Chronic obstructive airway disease	0	2 [3.9]	0.238

Table.5. Demographics

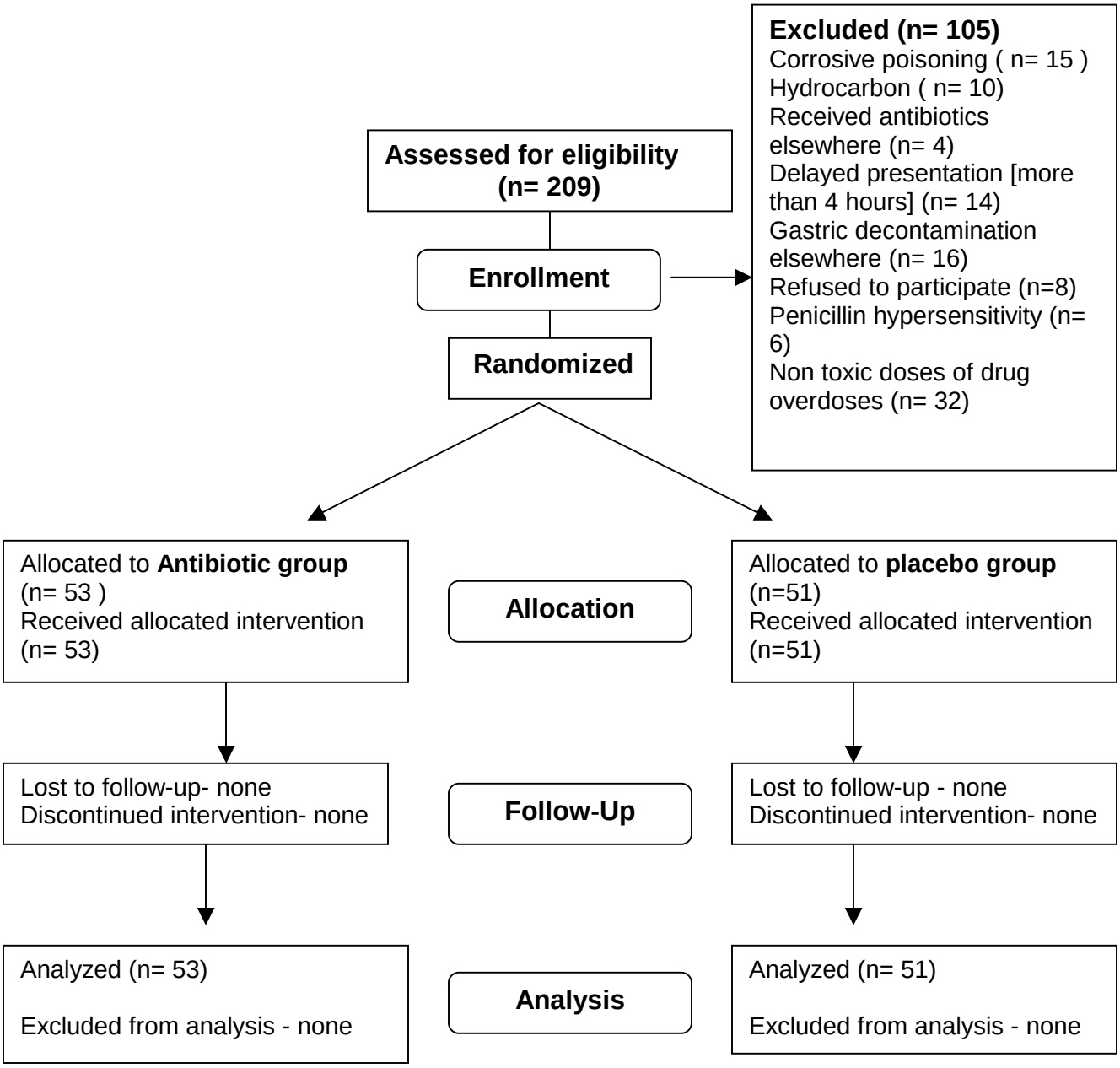

Figure 5. Trial profile

	Prophylactic antibiotic group N=53	**Placebo group N=51**	**p value**
Time to gastric lavage from poison ingestion [in minutes]	149 ± 63	160 ± 64	0.350
Systolic blood pressure At admission	122 ± 17	122 ± 21	0.736
Heart rate at admission	97 ± 17	100 ± 19	0.538
Saturation	95 ± 8	92 ± 15	0.917
GCS score	13 ± 3	13 ± 4	0.668
Intubation	17 [32.1]	15 [29.4]	0.769
Place of intubation Emergency room Ward Medical ICU	 10 6 1	 13 2 0	
Time to intubation in hours from admission	8 ± 14	7± 15	0.883
Admission Ward MICU	 42 11	 40 11	 0.919
APACHE II score	8 ± 5	9 ± 6	0.157
Enteral feeding	38	34	0.578
Stress ulcer prophylaxis	49	46	0.739

Table6. Clinical Characteristics at admission

	Prophylactic antibiotic group N=53	**Placebo group N=51**	**p value**
Hemoglobin mean	14.3 ± 2.4	14 ± 2.2	0.199
Total WBC count mean	12454 ± 4321	12684 ± 5125	0871
S.creatinine mean	0.9 ± 0.2	1.0 ±0.5	0.258
RBS mean	123 + 40	130 ± 37	0.106
Sodium mean	140 ± 3.8	140 ± 4.2	0.725
Potassium mean	3.5 ± 0.5	3.6 ± 0.5	0.715
Bicarbonate mean	20 ± 3	20± 3	0.547
Liver dysfunction	1	2	0.614
Pseudocholinesterase in OP	1442 ± 1765	1025 ± 1445	0.417

Table.7 Laboratory characteristics at admission

The mean age of the study population was 28 [range 16-70] in the prophylactic antibiotic group and 31 [range 14-70] in the placebo group. Majority of the patients were in the 21-30 age group (figure 6). Among the 104 patients included in the study, 59 (56.7%) were males and 45 (43.3 %) were females (figure7). All cases of the poisoning were due to deliberate self harm.

	Prophylactic antibiotic group	**Placebo group**
Poison type	53	51
Insecticides	**32**	**29**
organophosphate	23	18
organocarbamate	1	1
chlorinated hydrocarbon	1	2
pyrethroid	7	8
Plant poisons	**1**	**7**
oduvanthalai	1	3
oleander		4
Sedatives and antipsychotics	**4**	**3**
tricyclic	2	
barbiturates	1	1
benzodiazepines	1	1
antipsychotic		1
Rodenticides	**3**	**1**
Others	**13**	**11**
non ionic surfactant		1
unknown	5	4
other plant fertiliser	2	2
theophylline	1	
multiple drug overdosage	4	1
paracetamol		1
phenytoin		1
antidiabetic	1	1
Severity of OP poisoning		
Mild	7	9
Moderate	5	1
Severe	10	9

Table 8 Poison type and severity

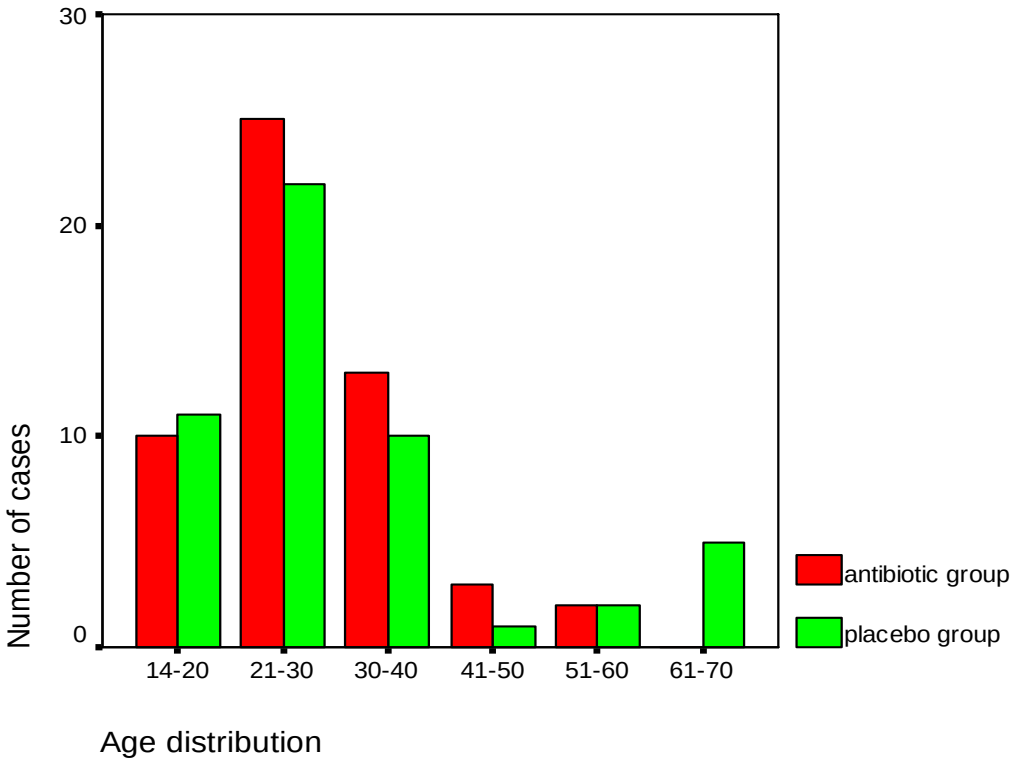

Figure. 6 Age distribution of the study patients.

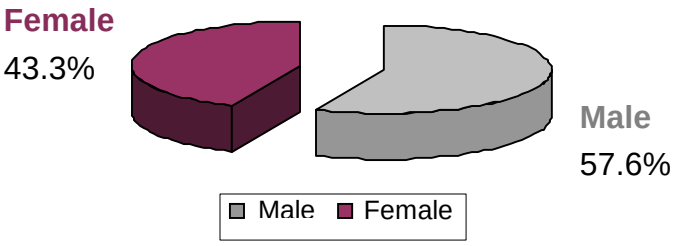

Figure 7 Sex distribution

Organophosphates were the most common compound involved in poisoning,39.4% of all poisonous compounds. (figure.8) Severity of organophosphate poisoning was evaluated using Namba's criteria (Annexure IV)

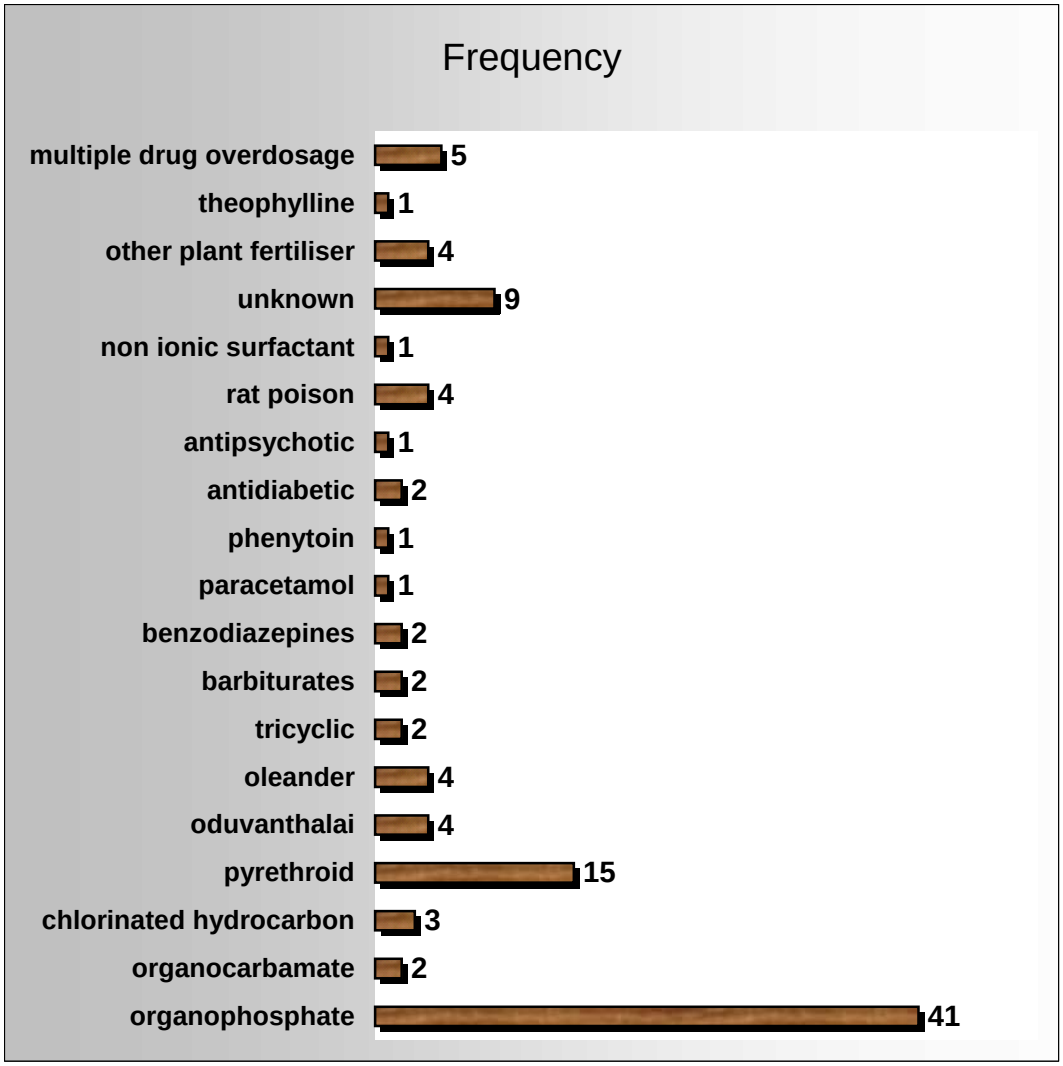

Figure.8 Frequency of poison consumed

II. PRIMARY OUTCOME

Overall, 11.5 % (n= 12) of the study population fulfilled the clinical criteria for pneumonia. Three belonged to the prophylactic antibiotic group and 9 belonged to the control or placebo group, **p= 0.056.** (figure.9). The risk ratio for patients receiving prophylactic antibiotics compared to patients receiving placebo was 0.32 [95% confidence interval, CI = 0.09 -1.12] (table 9). Although the risk reduction in terms of aspiration pneumonia

with antibiotics was 68%; this did not reach statistical significance. All cases of pneumonia occurred in the mechanical ventilated group.

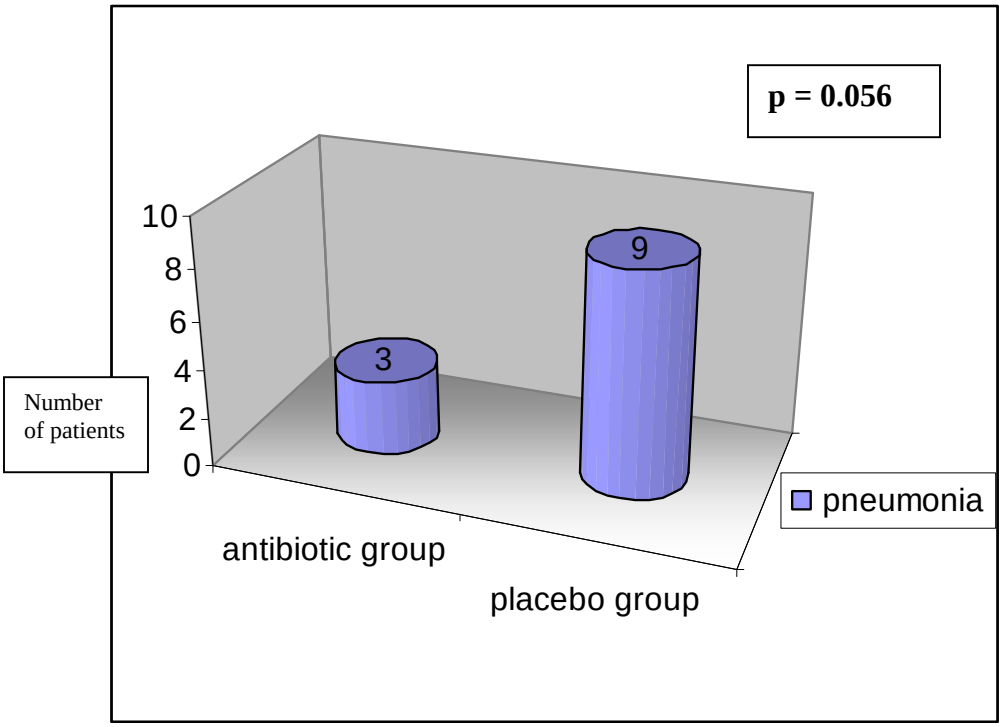

Figure 9 Pneumonia rates in antibiotic and placebo group

Only one patient had pneumonia occurring after four days of intubation. (late onset pneumonia).[52]

Outcomes	Antibiotic group	Placebo group	RR	95% CI	P value
Primary outcome [Pneumonia all patients]	**3**	**9**	**0.32**	**0.09 -1.12**	**0.056**
Mortality in all patients	5	5	0.96	0.30-3.13	1.00

Table. 9 Primary outcome and mortality

SECONDARY OUTCOMES

- There was no statistically significant difference between the antibiotic and placebo groups for all cause mortality (table 9), duration of hospital stay, MICU stay and mechanical ventilation. (table10)

A. Mortality

A total of ten patients enrolled in the study died. Both the prophylactic and control groups had equal number of deaths (5 each) (table9). Of the ten subjects who died, five had died due to pneumonia and sepsis, two died due to hypoxia related to tube block and other three due to effects of severity of poisoning. Five out of 12 patients who developed pulmonary infection died compared with five out of 92 patients without pulmonary infection. [p value=0.001]

B. Duration of hospital stay

Total duration of hospital stay was 6 $\pm$ 6 versus 6 $\pm$ 5 days for the prophylactic antibiotic and placebo groups respectively. (p=0.437). When analyzing patients who developed pneumonia and those who did not, total hospital stay was 13 $\pm$ 8 and 5 $\pm$ 5 respectively (p=0.000) which was statistically significant.

C. Duration of intensive care unit stay

Total duration of ICU stay was 9 ± 5 versus 8 ± 6 days for the prophylactic antibiotic and placebo groups respectively. (p=0.489)

	Antibiotic group	Placebo group	P value
Duration of hospital stay (in days)	6 ± 6	6 ± 6	0.437
Duration of ICU stay(in days)	9 ± 5	8 ± 6	0.489

Table. 10 secondary outcomes

D. Adverse drug reactions

No adverse drug reactions were recognized in patients receiving either intervention.

E. Microbiology

The isolates from the 12 patients who developed pneumonia is shown in the table. Both groups had equal number of gram positive organisms.

There was no statistical difference between the two groups for the gram negative organisms [p value=1.00] (table11)

Micro organism	**Number of**	**Antibiotic group**	**Placebo group**

	isolates	(n=3)	(n= 9)
Staphylococcus aureus	2	0	2
Alpha hemolytic streptococci	2	1	1
Staphylococcus Epidermidis	2	1	1
Morganella	1	0	1
Pseudomonas aeruginosa	1	0	1
Klebsiella sp	2	1	1
E. Coli	1	0	1
Other non fermenting gram negative bacteria	3	1	2
Total	14	4	10

Table 11 Isolated microorganisms in the 12 episodes of pulmonary infection

F. Treatment of Pneumonia

Empiric antibiotics were begun and were adjusted according to the culture and sensitivity results. Antibiotics that were given were cefepime, augmentin, aminoglycosides and metronidazole. These antibiotics were given as monotherapy or in combination.

III. SUB GROUP ANALYSIS

Since all pneumonias occurred in the ventilated population, a post hoc subgroup analysis was done for that group. The results are as follows.

A. Incidence of pneumonia in Ventilated patients

Out of 32 ventilated patients, 12 developed pneumonia, 3 in the antibiotic group and 9 in the placebo group. p value= 0.014. Distribution of ventilated patients among the two groups is shown in table12. The results were statistically significant. The calculated risk ratio for patients receiving prophylactic antibiotics compared to patients receiving placebo was 0.29 [95% confidence interval, CI=0.10 -0.89]. Absolute risk reduction was 43 giving a number needed to treat of 2.3. (table13)

			Total
	Antibiotic group	Placebo group	
ventilated	17	15	32
Not ventilated	36	36	72
Total	53	51	104

Table.12 Distribution of ventilated patients among the two groups

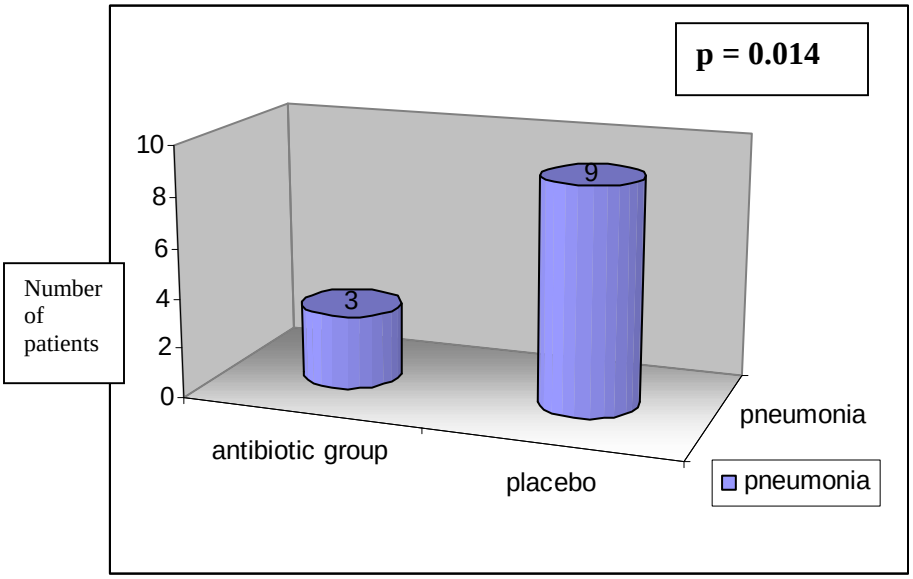

Figure 10 Pneumonia rates among ventilated patients

Outcomes	Antibiotic group	Placebo group	RR	95% CI	P value
Pneumonia in ventilated patients [Post hoc subgroup analysis]	3	9	0.29	0.10-0.89	0.014
Mortality in vetilated patients [Post hoc subgroup analysis]	5	5	0.88	0.32-2.46	1.00

Table.13 Pneumonia incidence and mortality in ventilated population

Duration of Mechanical ventilation, hospital and ICU stay in ventilated population

There was no statistically significant difference between the two groups for the duration of mechanical ventilation. Total duration of mechanical ventilation (mean ± SD) for the ventilated poisoned subjects were 7 ± 6 versus 7 ± 5 days for the prophylactic antibiotic and placebo groups respectively. (p=0.856) (table14). Duration of mechanical ventilation prior to the development of pulmonary infection was 2.7 ± 2.9 and 2.2 ± 1 days for the antibiotic prophylactic and control groups respectively (p=0.631). There was no statistically significant difference between the two groups for the duration of hospital stay and intensive care unit stay (table15).

	Antibiotic group	Placebo group	P value
Duration of mechanical ventilation (in days)	7 ± 6	7 ± 5	0.856

Table.14 Duration of mechanical ventilation

	Antibiotic group	Placebo group	P value
Duration of hospital stay	11± 9	12 ± 7	0.677
Duration of ICU stay	9 ± 5	9 ± 6	0.970

Table.15 Duration of hospital stay and icu stay for ventilated subjects

Kaplan Meier curve for patients remaining free of pneumonia in ventilated patients is shown in the figure 11. Among the ventilated patients, significantly fewer patients who received antibiotics acquired infections.

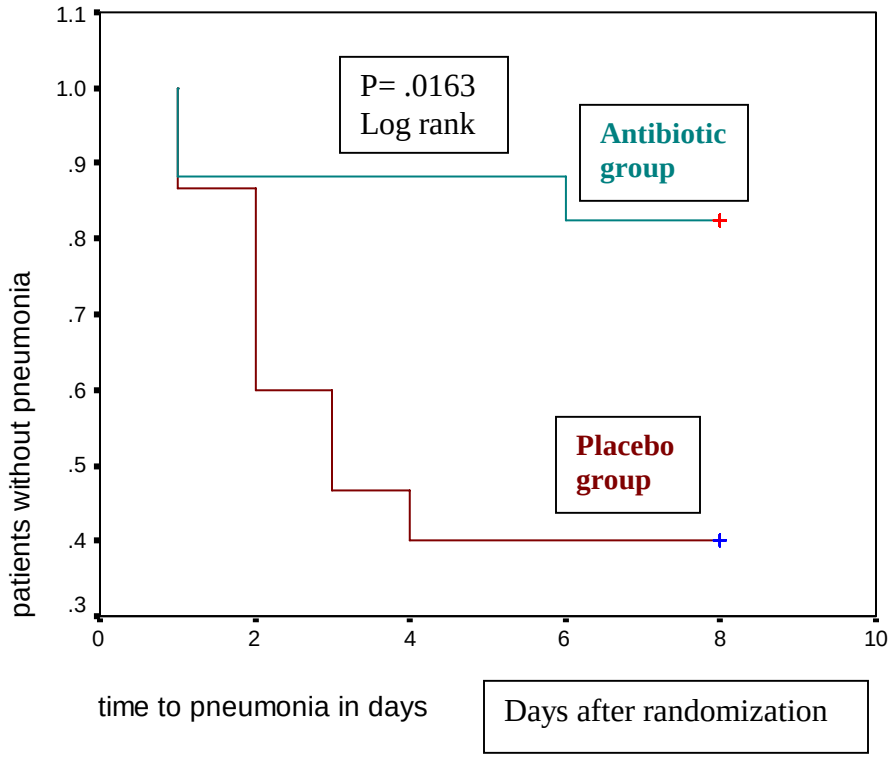

Figure 11 Kaplan Meier curve for patients remaining free of pneumonia in ventilated patients for the two groups

Sepsis in ventilated group

A total of 9 patients fulfilled the standard criteria for sepsis (Annexure V) in the ventilated population. Two belonged to the antibiotic group and seven belonged to the placebo group. (p=0.049)

Risk factors for developing pneumonia

Univariate analysis identified male sex and GCS <8 as predictors of pneumonia in the entire cohort of poisoned subjects. Multivariate analysis

could not be done because number of patients with pneumonia was too small.

DISCUSSION

This study, a prospective randomized double blind placebo control trial of short course prophylactic antibiotics (three doses of crystalline penicillin and single dose of Levofloxacin), suggested a trend towards a reduction of incidence of aspiration pneumonia with antibiotic prophylaxis in patients presenting with poisoning (p=0.056). It is important however, to note that all pneumonias occurred in mechanically ventilated patients. This observation could reflect the fact that the sicker, critically ill patient is particularly at risk for aspiration and its consequences. A post hoc analysis in this subgroup of mechanically ventilated patients showed a relative risk reduction of 71% (95% confidence interval, CI 0.10-0.89) and an absolute risk reduction of 43% with antibiotics compared to the placebo. Thus, the number of patients who needed to be treated (NNT) to avoid one episode of pneumonia in poisoned subjects needing ventilatory support was an impressive 2.3 patients.

Our findings assume importance given that this is the first randomized double blind placebo controlled trial of short course antibiotic prophylaxis in patients presenting with poisoning.

The impact of short courses of systemic antibiotic prophylaxis in reducing the incidence of pneumonia has been studied in other clinical situations (table16). In a randomized controlled trial by Sirvent et al[13], short term antibiotic prophylaxis (two single cefuroxime doses 1500 mg each 12 hour apart after intubation was demonstrated to significantly

reduce the occurrence of pneumonia in patients with coma. The occurrence of pneumonia was 50% in the control group and 24% in the cefuroxime group (a 52% relative risk reduction). When considering early onset pneumonia which accounted for 70% of all pneumonias, the relative risk reduction was 56% (36% controls, 16% cefuroxime group). The cohort in the above study consisted of previously well individuals who required mechanical ventilation following head injury or stroke and is comparable in some ways to our patient population.

In another single centre prospective open study[14] a three day prophylaxis with ampicillin –sulbactam [3gm every 6 hours for three days] significantly reduced the occurrence of early onset pneumonia in critically ill comatose mechanically ventilated patients. The risk reduction for pneumonia again was impressive at 64 % and similar to that obtained for the mechanical ventilated subjects in our study. The open label study design and small sample size (19 in each group) were considered to be the major limitations of that study.

Prophylactic antibiotics, on the other hand, may not be without adverse effects. Ewig et al[70] in a prospective observational study showed that prolonged found that prolonged antibiotic prophylaxis independently

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Study	Antibiotic regimen and duration	Type of patients	Number of patients in the study	Number of patients in each group [placebo/ antibiotic]	Pneumonia incidence in the control / standard therapy group	Pneumonia incidence in the antibiotic group	Relative risk reduction	P value
Sirvent et al [13]	Two single doses of cefuroxime 1500mg each12 hours apart	individuals who required mechanical ventilation following head injury or stroke	100	50 / 50	25 / 50	12 / 50	52%	.007
Acquarolo et al[14]	ampicillin–sulbactam 3gm every 6 hours for 3 days	critically ill comatose mechanically ventilated patients	38	19 / 19	11 / 19	4 / 19	64 %	.022
Mechanical ventilated patients in our study	Three doses of crystalline penicillin (20 lakh units) four hours apart and a single dose of levofloxacin (500 mg)	Poisoned subjects who require mechanical ventilation	32ventilated patients	15 / 17	9 / 15	3 / 17	71%	0.014

Table16 Comparison of our study with other studies on short course prophylactic antibiotics in critically ill patients

predicted late onset pneumonia. The mean duration of treatment was 5 days in that study. In another study, Hoth et al[71] in a retrospective observational study found that for patients receiving prolonged prophylactic antibiotics (mean, 8 days) the first pneumonia was diagnosed later, the causative organisms were more likely to be resistant or gram-negative bacteria, and the occurrence of antibiotic complications was two times greater than for patients who did not receive antibiotic prophylaxis.

Several investigators have used combinations of topical and parenteral antibiotics for selective digestive decontamination in ICU with a view to reducing the incidence of nosocomial pneumonia. Liberati et al[71] in a recent meta-analysis of randomized control trials comparing different forms of antibiotic prophylaxis (topical oral non-absorbable, systemic, combined topical and systemic) found a strong reduction in respiratory tract infection and mortality when a combination of topical and systemic antibiotics were used. A recent large randomized control trial[73] comparing critically ill medical patients receiving oral topical non-absorbed antibiotics combined with an initial 4-day course of intravenous cefotaxime with controls receiving standard treatment also found decreased ICU and hospital mortality in patients receiving antibiotic prophylaxis. The studies support the use of prophylactic antibiotics in the prevention of nosocomial infections, particularly pneumonias. A major difference however between these studies and our current study was the clinical situation (poisoning) as well as the duration of antibiotic prophylaxis (short duration). The total

cost of the prophylactic antibiotic regimen used in our study was about Rs.100 \- per patient, a likely cost saving approach if one was to consider the costs of treatment of one episode of pneumonia.

No statistically significant differences were observed (although there was a favorable trend) with regard to primary outcome when comparing the study population and the control group in our study. This lack of difference could be explained by several reasons including sample size limitations. Prior to the start of the study, an audit of the previous ten months showed a pneumonia incidence of about 35% in poisoning subjects. In our prospective study, the pneumonia rate in the control group was only 17.6%. This decrease in the pneumonia incidence in the control group could have affected the effective sample size and power of the study. We speculated the decrease in pneumonia rates to be due to the following reasons. The population in the audit study prior to the clinical trial also included subjects who had received gastric lavage elsewhere and this may have contributed to the higher incidence. Our study excluded patients who had received gastric decontamination elsewhere. In a recent observational study[12] in Sri Lanka, an improperly conducted gastric lavage without adherence to the recommended methods was found to carry a high risk of aspiration and other complications including death. This study done also noted that several hospitals in the South East Asian region were not performing lavage as recommended and that frequent and serious complications frequently

resulted. In our study, recommended methods (Annexure VI) for lavage was strictly adhered to by the emergency room nurses, who were trained alike. This could have resulted in a decreased incidence of pneumonia in the control group in our study.

No differences were observed with regard to secondary outcomes in our study. The lack of difference in secondary outcomes when comparing the two groups could be explained by factors other than pneumonia that accounted for morbidity and mortality. Of the five patients who died in the antibiotic group, only one (20%) died due to pneumonia, whereas of the five deaths in control group, four (80%) had died due to pneumonia. The remaining four deaths in the antibiotic group were due to other factors such as hypoxia related to tube block in two patients. As mentioned earlier when we compared patients with pneumonia with those who did not develop it, there was a reduction in total duration of hospital stay.

An important question in any prophylactic antibiotic trial that needs to be addressed is whether the prophylaxis may increase the emergence of multidrug resistant bacteria and adversely affect the outcome. In this present trial, both the control and placebo group had nearly equal number of gram positive bacteria isolated. Control group had slightly more gram negative bacteria and non fermenting gram negative rods. None of the organisms isolated in the antibiotic group was multidrug

resistant. This justifies the use of Levofloxacin in our trial to cover gram negative bacteria.

This study answers certain questions and leaves us with several unanswered questions. In our study, prophylactic regimen was intended to give maximum protection during the initial 12 hours following hospitalization. Whether a protective effect against is provided by a longer duration of prophylaxis of 48- 72 hours needs to be studied. Again the role for prophylaxis in unintubated non mechanical ventilated poisoning patients needs to be clarified. Due to difficulties in doing anaerobic culture and financial constraints, anaerobic cultures were not done as a part of our study. Also we did not do a formal cost effective analysis in the ventilated patients. Whether the prophylactic antibiotic therapy modifies the cost of treatment, hospital stay and indirect costs needs to be addressed.

The major implications of our results could be the following.

A. From the demographic profile and baseline characteristics of our study, poisoning appears to be a major problem in the younger age groups especially in males. Highly toxic compounds such as organophosphates are easily available and often are common household items. Policies such as minimum pesticide list should be made to restrict the availability of such highly toxic agents. Steps may be taken to prevent poisoning and

repeated suicidal attempts which in turn will reduce consequent morbidity and mortality associated with it.

B. Overall, there was a trend to a reduction in the incidence of pneumonia in poisoned subjects randomized to the prophylactic antibiotic group. The significant reduction in the incidence rates of pneumonia in the subgroup analysis of mechanical ventilated patients has important implications.

1) With the mortality and morbidity associated with pneumonia in ventilated subjects being high, any intervention that could reduce the incidence of pneumonia is worthy of study and consideration. The benefits of antibiotic prophylaxis in this subgroup of ventilated patients thus have clinical as well as financial implications.

2) A very short course antibiotic prophylaxis of three doses of penicillin and a single dose of Levofloxacin may be less likely to decontaminate the gut and favor the colonization of more pathogenic bacteria, although this was not looked at in this study

C. This study has shown that patients who developed pneumonia had significantly increased mortality rates and duration of hospitalization. Hence measures to reduce pneumonia are of importance.

Limitations

The major limitations in our study included the following.

1. Sample size limitations since the end point of our study was the reduction of the incidence of pneumonia.

2. Power of the study could have been affected since the pneumonia rate in the control group was less when compared to that at the beginning of the study. In fact, the recalculated power using incidence rates in the present study was 70%. A much larger trial with about 103 patients in each arm would be needed to demonstrate a benefit using incidence rates in the present study, assuming an Alpha error of 5% and a power of 80% by a one-tailed test.

3. Anaerobic cultures were not routinely done due to difficulties in sampling and cost constraints.

4. It was clinically impossible to differentiate between aspiration and early onset ventilator associated pneumonia in our study. The incidence of late onset pneumonia was small suggesting that aspiration at the time of poisoning or during gastric lavage at least predisposed to the development of early onset pneumonia.

Conflicts of interest: None

Financial disclosure: This study was done with the help of the generous grand provided by the FLUID Research Committee of the Christian Medical College and Hospital, Vellore.

Conclusions

In summary, the present study demonstrates that the administration of a combination of three doses of intravenously administered crystalline penicillin and a single dose of Levofloxacin resulted in a trend towards a reduction in the incidence of pneumonia in poisoned patients randomized to the prophylactic antibiotic group.

Antibiotic prophylaxis is probably an effective prophylactic strategy for the prevention of pneumonia in mechanically ventilated poisoned subjects although the benefit did not reach statistical significance in the whole cohort of poisoned patients.

These observations justify the conduct of a larger prospective study to evaluate the role of prophylactic antibiotics in poisoned patients. If such an intervention would reduce the morbidity and mortality, it would have great implications especially in our country where resources are limited.

BIBLIOGRAPHY

(Referenced in Vancouver style)

1. Jeyaratnam J. Acute pesticide poisoning: a major global health problem. World Health Stat Q 1990;43:139-44.
2. Eddleston M, Sudarshan K, Senthilkumaran M, Reginald K, Karalliedde L, Senarathna L et al. Patterns of hospital transfer for self-poisoned patients in rural Sri Lanka: implications for estimating the incidence of self-poisoning in the developing world. Bull World Health Organ 2006;84:276-82
3. Eddleston M. Patterns and problems of deliberate self-poisoning in the developing world. Q J Med 2000;93:715-31.
4. Tsao TC, Juang YC, Lan RS, Shieh WB, Lee CH. Respiratory failure of acute organophosphate and carbamate poisoning. Chest 1990;98:631-6.
5. Sungur M, Guven M. Intensive care management of organophosphate insecticide poisoning. Critical Care 2001;5:211-5.
6. Shannon M, Lovejoy FH Jr. Pulmonary consequences of severe tricyclic antidepressant ingestion. J Toxicol Clin Toxicol 1987;25:443-61
7. Moll J, Kerns W 2nd, Tomaszewski C, Rose R. Incidence of aspiration pneumonia in intubated patients receiving activated charcoal.J Emerg Med 1999;17:279-83.
8. Liisanantti J, Kaukoranta P, Martikainen M, Ala-Kokko T. Aspiration pneumonia following severe self-poisoning. Resuscitation 2003;56:49-53
9. Leroy O, Vandenbussche C, Coffinier C, Bosquet C et al.Community-acquired aspiration pneumonia in intensive care units. Epidemiological and prognosis data. Am J Respir Crit Care Med 1997;156:1922-9.
10. Merigian KS, Woodard M, Hedges JR, Roberts JR, Stuebing R, Rashkin MC. Prospective evaluation of gastric emptying in the self-poisoned patient. Am J Emerg Med 1990; 8:479-83

11. Marik PE. Aspiration pneumonitis and aspiration pneumonia. N Engl J Med 2001;344:665-71
12. Eddleston M, Haggalla S, Reginald K,Sudarshan K, Senthilkumaran M, Karalliedde L et al. A survey of gastric lavage for intentional self-poisoning in the developing world. Clinical Toxicology 2006; (in press) Available from:http://www.sactrc.org/
13. Sirvent JM, Torres A, El-Ebiary M, Castro P, de Batlle J, Bonet A. Protective effect of intravenously administered cefuroxime against nosocomial pneumonia in patients with structural coma.Am J Respir Crit Care Med 1997;155:1729-34
14. Acquarolo A, Urli T, Perone G, Giannotti C, Candiani A, Latronico N. Antibiotic prophylaxis of early onset pneumonia in critically ill comatose patients. A randomized study.Intensive Care Med 2005;31:510-6.
15. Klaassen C, editor. In: Casarett and Doull's toxicology. The basic science of poisons. 6th ed. McGraw-Hill Professional; 2001. p. 3,4, 1090.
16. Hodgson E, editor. A text book of modern toxicology. 3rd ed. John Wiley & Sons; 2004. p. 33,34.
17. Buckley NA, Karalliedde L, Dawson A, Senanayake N, Eddleston M. Where is the evidence for the management of pesticide poisoning – is clinical toxicology fiddling while the developing world burns? J Toxicol Clin Toxicol 2004;42:113-6.
18. Mier L, Dreyfuss D, Darchy B, Lanore JJ et al.Is penicillin G an adequate initial treatment for aspiration pneumonia? A prospective evaluation using a protected specimen brush and quantitative cultures.Intensive Care Med 1993;19:279-84.
19. Marik PE, Careau P. The role of anaerobes in patients with ventilator-associated pneumonia and aspiration pneumonia: a prospective study. Chest 1999;115:178-83.

20. Greaves I, Goodacre S, Grout P. Management of drug overdose in accident and emergency departments in the United Kingdom. J Accident Emerg Med 1996;13:46-8.
21. Hawton K, Fagg J, Simkin S, Bale E, Bond A. Trends in deliberate self-harm in Oxford, 1985-1995. Implications for clinical services and the prevention of suicide. Br J Psychiatry 1997; 171:556-60.
22. Agarwal P, Handa R, Wali JP; Common poisoning in India; Journal of Forensic Medicine & Toxicology 1998;15:73-9.
23. Batra AK, Keoliya AN, Jadhav GU. Poisoning: an unnatural cause of morbidity and mortality in rural India. J Assoc Physicians India. 2003;51:955-9.
24. Eddleston M, Phillips MR. Self poisoning with pesticides. BMJ 2004;328:42-4.
25. Phillips MR, Li X, Zhang Y. Suicide rates in China, 1995-99. Lancet 2002;359:835-40
26. Townsend E, Hawton K, Harriss L, et al. Substances used in deliberate selfpoisoning 1985–1997: trends and associations with age, gender, repetition and suicide intent. Soc Psychiatry Psychiatr Epidemiol 2001;36:228-34.
27. Hawton K, Townsend E, Deeks J, et al. Effects of legislation restricting pack sizes of paracetamol and salicylate on self poisoning in the United Kingdom: before and after study. BMJ 2001;322:1203-7.
28. Srivastava A, Peshin SS, Kaleekal T, Gupta SK .An epidemiological study of poisoning cases reported to the National Poisons Information Centre, All India Institute of Medical Sciences, New Delhi. Hum Exp Toxicol 2005;24:279-85.
29. Siwach SB, Gupta A. The profile of acute poisonings in Harayana-Rohtak Study. J Assoc Physicians India1995;43:756-9
30. Singh B, Unnikrishnan B. A profile of acute poisoning at Mangalore (South India). J Clin Forensic Med 2006;13:112-6.

31. Unnikrishnan B, Singh B, Rajeev A. Trends of acute poisoning in south Karnataka. Kathmandu Univ Med J 2005;3:149-54.
32. Batra AK, Keoliya AN, Jadhav GU. Poisoning: an unnatural cause of morbidity and mortality in rural India.J Assoc Physicians India. 2003;51:955-9.
33. Thomas M, Anandan S, Kuruvilla PJ, Singh PR, David S. Profile of hospital admissions following acute poisoning--experiences from a major teaching hospital in south India.Adverse Drug React Toxicol Rev 2000;19:313-7.
34. Peter JV, Cherian AM. Organic insecticides. Anaesth Intensive Care 2000; 28:11-21.
35. Zine KU, Mohanty AC. Pattern of acute poisoning at Indira Gandhi Medical College and Hospital, Nagpur. J Ind Aca For Med 1998;20:37-9
36. Gunnell D, Ho D, Murray V. Medical management of deliberate drug overdose: a neglected area for suicide prevention? Emerg Med J 2004;21:35-8
37. Sudarsanam TD, Pichaimuthu K, Zacharaiah A, John G. Oximes in acute organophosphate poisoning. Crit Care Med 2006;34:2265.
38. Kasper DL, Fauci AS, Longo DL, Braunwald E, Hauser SL, Larry J In:Harrisons principles of internal medicine.16th ed The McGraw-Hill Companies,Inc; 2005. p. 2582.
39. Heard K. Gastrointestinal decontamination. Med Clin North Am 2005; 89:1067-78
40. Knight PR, Rutter T, Tait AR, Coleman E, Johnson K.Pathogenesis of gastric particulate lung injury: a comparison and interaction with acidic pneumonitis.Anesth Analg 1993;77:754-60.
41. Kennedy TP, Johnson KJ, Kunkel RG, Ward PA, Knight PR, Finch JS.Acute acid aspiration lung injury in the rat: biphasic pathogenesis. Anesth Analg. 1989;69:87-92.

42. Rotta AT, Shiley KT, Davidson BA, Helinski JD, Russo TA, Knight PR.Gastric acid and particulate aspiration injury inhibits pulmonary bacterial clearance. Crit Care Med 2004;32:747-54.
43. Roy TM, Ossorio MA, Cipolla LM, Fields CL, Snider HL, Anderson WH. Pulmonary complications after tricyclic antidepressant overdose. Chest 1989;96:852-6.
44. Aldrich T, Morrison J, Cesario T. Aspiration after overdosage of sedative or hypnotic drugs. South Med J 1980;73:456-8.
45. Jay SJ, Johanson WG Jr, Pierce AK. Respiratory complications of overdose with sedative drugs. Am Rev Respir Dis 1975 ;112:591-8.
46. Paudyal BP. Poisoning: pattern and profile of admitted cases in a hospital in central Nepal.JNMA J Nepal Med Assoc 2005;44:92-6.
47. El-Solh AA, Pietrantoni C, Bhat A, Aquilina AT, Okada M, Grover V et al. Microbiology of severe aspiration pneumonia in institutionalized elderly. Am J Respir Crit Care Med 2003;167:1650-4.
48. Terpenning MS, Taylor GW, Lopatin DE, Kerr CK, Dominguez BL, Loesche WJ. Aspiration pneumonia: dental and oral risk factors in an older veteran population. J Am Geriatr Soc 2001;49:557-63.
49. Lorber B, Swenson RM. Bacteriology of aspiration pneumonia. A prospective study of community- and hospital-acquired cases.Ann Intern Med 1974;81:329-31
50. Bartlett JG, Gorbach SL, Finegold SM. The bacteriology of aspiration pneumonia. Am J Med. 1974;56:202-7.
51. Luna CM, Blanzaco D, Niederman MS, Matarucco W, Baredes NC, Desmery P et al. Resolution of ventilator-associated pneumonia: prospective evaluation of the clinical pulmonary infection score as an early clinical predictor of outcome. Crit Care Med 2003;31:676-82.
52. Hunter JD.Ventilator associated pneumonia. Postgrad Med J 2006;82:172-8

53. Hickling KG, Howard R. A retrospective survey of treatment and mortality in aspiration pneumonia. Intensive Care Med 1988;14:617-22.
54. Cameron JL, Mitchell WH, Zuidema GD: Aspiration pneumonia. Clinical outcomes following documented aspiration. Arch Surg 1973;106:49-53.
55. Jones J.Risk and outcome of aspiration pneumonia in a city hospital.J Natl Med Assoc 1993l;85:533-6.
56. Isbister GK, Downes F, Sibbritt D, Dawson AH, Whyte IM.Aspiration pneumonitis in an overdose population: frequency, predictors, and outcomes.Crit Care Med 2004; 32: 88-93.
57. Christ A, Arranto CA, Schindler C, Klima T, Hunziker PR, Siegemund M, Marsch SC, Eriksson U, Mueller C. Incidence, risk factors, and outcome of aspiration pneumonitis in ICU overdose patients. Intensive Care Med. 2006 Jul 7; [Electronic publication; ahead of print]
58. Vucinic S.Risk factors for the development of pneumonia in acute psychotropic drugs poisoning. Vojnosanit Pregl. 2005 ;62:715-23
59. Adnet F, Borron SW, Finot MA, Minadeo J, Baud FJ. Relation of body position at the time of discovery with suspected aspiration pneumonia in poisoned comatose patients.Crit Care Med. 1999; 27:745-8
60. Adnet F, Baud F. Relation between Glasgow Coma Scale and aspiration pneumonia. Lancet 1996; 348:123-4.
61. Bartlett JG. Treatment of anaerobic pulmonary infections. J Antimicrob Chemother 1989;24:836-40.
62. Johnson JL, Hirsch CS. Aspiration pneumonia. Recognizing and managing a potentially growing disorder. Postgrad Med 2003;113:99-102,105-6,111-2.
63. Krueger WA, Lenhart FP, Neeser G, Ruckdeschel G, Schreckhase H, Eissner HJ et al. Am J Respir Crit Care Med. 2002;166:1029-37.

64. Gold HS, Moellering RC Jr. Antimicrobial-drug resistance.N Engl J Med 1996;335:1445-53.
65. Schwartz B, Bell DM, Hughes JM. Preventing the emergence of antimicrobial resistance. A call for action by clinicians, public health officials, and patients. JAMA 1997;278:944-5
66. Smith JW, Johnson JE, Cluff LE. Studies on the epidemiology of adverse drug reactions. II. An evaluation of penicillin allergy.N Engl J Med 1966;274:998-1002.
67. Parker CW.Allergic reactions in man. Pharmacol Rev 1982;34:85-104.
68. Zadik PM, Moore AP. Antimicrobial associations of an outbreak of diarrhoea due to Clostridium difficile. J Hosp Infect 1998;39:189-93.
69. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections, 1988.Am J Infect Control 1988;16:128-40.Erratum in: Am J Infect Control 1988;16:177.
70. Ewig S, Torres A, El-Ebiary M, Fabregas N, Hernandez C, Gonzalez J, et al. Bacterial colonization patterns in mechanically ventilated patients with traumatic and medical head injury. Incidence, risk factors, and association with ventilator-associated pneumonia.Am J Respir Crit Care Med 1999;159:188-98.
71. Hoth JJ, Franklin GA, Stassen NA, Girard SM, Rodriguez RJ, Rodriguez JL. Prophylactic antibiotics adversely affect nosocomial pneumonia in trauma patients.J Trauma 2003;55:249-54.
72. Liberati A, D'Amico R, Pifferi, Torri V, Brazzi L..Antibiotic prophylaxis to reduce respiratory tract infections and mortality in adults receiving intensive care.Cochrane Database Syst Rev. 2004.
73. de Jonge E, Schultz MJ, Spanjaard L, Bossuyt PM, Vroom MB, Dankert J et al. Effects of selective decontamination of digestive tract on mortality and acquisition of resistant bacteria in intensive care: a randomised controlled trial. Lancet 2003;362:1011-6.

ANNEXURE I

ETHICS COMMITTEE APPROVAL CERTIFICATE

CHRISTIAN MEDICAL COLLEGE
VELLORE - 632 002. INDIA.
INSTITUTIONAL REVIEW BOARD
(ETHICS COMMITEE)

Dr. D. Daniel Ezhilarasu, M.Sc., Ph.D.,
Chairman.

Dr. B. Antonisamy, M.Sc., Ph.D.,
Secretary

Institutional Review Board (Ethics Committee) of CMC, Vellore

Ref: IRB(EC)5/08/05 September 9, 2005

To Whom It May Concern

The meeting of the Institutional Review Board (Ethics Committee) of the Christian Medical College, Vellore, was held on 19th August 2005. The committee discussed the ethical aspects of the proposal and approved the project proposal entitled "Impact of short course prophylactic antibiotics in poisoning" by Dr. John Jose, PG Registrar, Medicine II, Dr. Debashish Danda, Medicine II, to be carried out in the Department of Medicine Unit II.

B Antonisamy

Dr. B.Antonisamy
Secretary,
Institutional Review Board
(EthicsCommittee)

September 9, 2005.
Secretary,
Institutional Review Board,
(Ethics Committee)
Christian Medical College & Hospital,
Vellore-632 004. Tamil Nadu. India.

TEL : 0416 - 2284205, 2262703 Fax : 0416 - 2262703, 2262788
e-mail : biostats@cmcvellore.ac.in

ANNEXURE II

INFORMED CONSENT DOCUMENT

Study Title: Impact of short course prophylactic antibiotics in poisoning

This information and consent form is meant for the closest kin of the patient
This is a clinical trial, a type of research study. Clinical trials include only people who choose to take part. Please take your time to make your decision about taking part.

.

1. Why is this study being done?

Standard treatment for any poisoning presenting early to emergency department includes gastric lavage unless there are no contraindications. This procedure carries a high risk of aspiration and development of lower respiratory infection.

The purpose of this study is to compare the effects, good and/or bad, of antibiotic [crystalline penicillin injection + levofloxacin] with [placebo] on the patient and to find out which is better in preventing lower respiratory tract infection. In this study, patient will get either the [drug/intervention] or the [placebo]. He/she will not get both.

Currently no antibiotics are given during gastric lavage by some medicine departments; whereas others prefer giving antibiotics. Drugs–penicillin and levofloxacin are common antibiotics given for the treatment of lower respiratory infection. They are not new agents being tested.

3. How many people will take part in the study?

A total of 102 people will take part in the study.

4. What will happen if the patient take part in this research study?

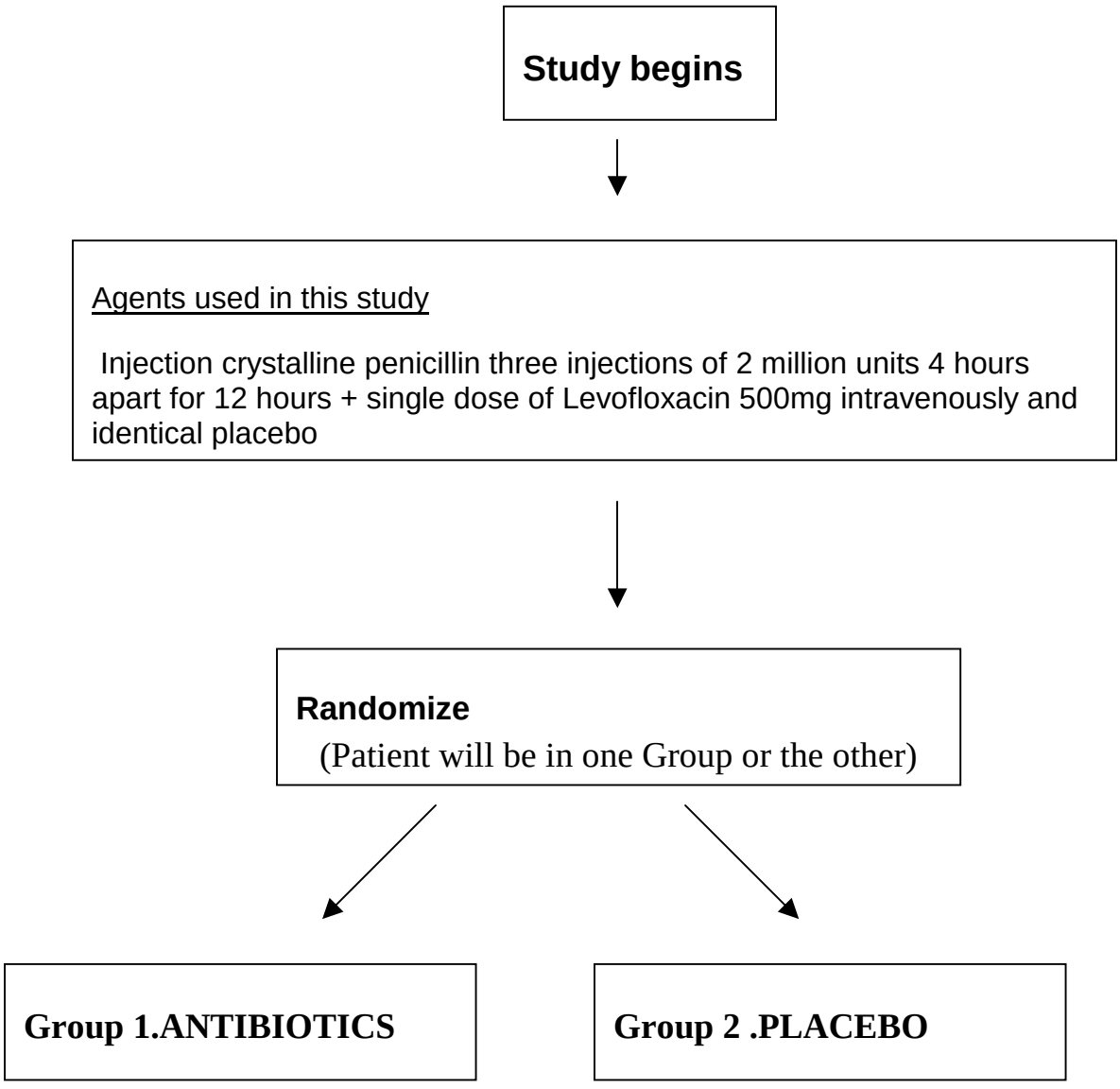
Patient will be “randomized” into one of the study groups described below. Randomization means that patient is put into a group by chance. Neither you nor your doctor can choose the group patient will be in. Patient will have an equal chance of being placed in any group.

If patient is in group 1 (often called "Arm A") you will receive antibiotics -3 intravenous injections of penicillin 4 hours apart and a single intravenous of levofloxacin in a 12 hour period.

If patient is in group 2 (often called "Arm B’) you will receive a placebo. Placebos are inert substances i.e. they don’t have any effects (good or bad) on the body.

Study Plan

Another way to find out what will happen to you during the study is to read the chart below. Start reading at the top and read down the list, following the lines and arrows.



5. How long will patient be in the study?

Till discharge from hospital/MICU

6. Can patient stop being in the study?

Yes. You can decide to stop at any time.

7. What side effects or risks can occur from being in the study?

Side effects may occur while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, we don't know all the side effects that may happen. Side effects may be mild or very serious. Many side effects go away soon after you stop taking the intervention. There also is a risk of death.

8. Are there benefits to taking part in the study?

While we hope intervention will be more useful in preventing, there is no proof of this yet. We do know that the information from this study will help us learn more about intervention as an agent in lower respiratory tract infection prevention

9. Will patients' medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, name and other personal information will not be used.

Consent Document

I, ----------(name) closet kin of ----------(name) (relation) have been given a copy of all pages of this form. I have read it or it has been explained to me in my own language. I understand the information and have had my questions answered. I agree for the patient to take part in this study.

Closest kin's signature _____

Date _____

ANNEXURE III

DATA ABSTRACTION FORM

Title: Impact of short course prophylactic antibiotics in poisoning

1. DEMOGRAPHIC DETAILS **Screening date:**

Name: Hospital number: Medical Record Department number:

Age: Sex: Unit:

Address:

INCLUSION CRITERIA MET	YES / NO	**EXCLUSION CRITERIA MET**	YES / NO
INFORMED CONSENT OBTAINED	YES / NO		

2. **RECRUITMENT No.** **INTERVENTION No.**

---

3. Past medical details

Diabetes mellitus	Yes / No
Hypertension	Yes / No
Smoking	Yes / No
Alcoholism	Yes / No
Asthma/Chronic obstructive pulmonary airway disease	Yes / No
Past history of pulmonary tuberculosis	Yes / No
Ischemic heart disease	Yes / No
Congestive cardiac failure	Yes / No

---

4. Pre hospital details and details of poisonous substance ingested

Poison / substance consumed:
Amount consumed:
Date and time of consumption:
Reason for consumption:
Was patient unconscious on discovery Yes / No
Other relevant history:

---

5. Emergency room details

Time to presentation to emergency room from ingestion [in hours]:

Examination details at the time of admission

Blood pressure	Heart rate	Respiratory rate	GCS	Saturation

In case of organophosphate poisoning : mild / moderate / severe

Other salient examination findings

Time to gastric lavage:
Activated charcoal: **Yes / No** **single / multidose**
Place of intubation: ER/ ward / MICU
Time to intubation in hours:
Lavage performed on intubated / un-intubated patient. GCS at the time of lavage:

---

6. Place of admission: ward/ MICU/ ward then MICU
Date of admission: Date of discharge:
Early enteral feeding: Yes / No
NG tube insertion: Yes / No
Stress ulcer prophylaxis: Yes / No
Re-intubation Yes / No date:

---

7. For organophosphate
Dose and duration of atropine
Intermediate syndrome Yes / No Duration

---

8. For patients admitted into medical ICU
Time to MICU admission:
APACHE II score at admission:
SAPS score:
TISS:
Duration of MICU stay:
Tracheostomy: Yes / No If yes, tracheostomy day

---

9. Investigations

At admission: Hemoglobin: total WBC count: differential WBC count
Random blood sugar: S. creatinine: S.sodium: S. potassium: S.bicarbonate:

Liver function tests:
Pseudocholinesterase levels in organophosphate poisoning:

Arterial blood gas

DATE/DAY							
FiO2/PEEP							
pH							
Pco2							
Po2							
HCO3							
ABE							
SaO2							

WBC counts

TC					
N					
L					
Ba					
E					
M					
BF					
META/MYELO					

Chest Radiograph: Normal / abnormal

Baseline	48 Hour	72 Hour	96 Hour	168 Hour

Secretions Purulent Yes / No

Baseline	48 Hour	72 Hour	96 Hour	168 Hour

Temperature

Baseline	48 Hour	72 Hour	96 Hour	168 Hour

Culture if done
Antibiotic

PATHOGEN 1						
PATHOGEN 2						
PATHOGEN 3						
PATHOGEN 4						
PATHOGEN 5						

---

10. Fulfilling criteria for pneumonia: Yes / No

Time from lavage to pneumonia:
If ventilated, time from ventilation to pneumonia:
Time to resolution:
Antibiotic used to treat pneumonia
Number of antibiotic days:

Duration of mechanical ventilation [days]: CPIS scores in ventilated patients:

11. MICU outcome: alive / dead / discharged at request Duration of ICU stay [days]:

Hospital outcome: alive / dead / discharged at request Duration of hospital stay [days]:

Any other nosocomial infection: Sepsis : Yes / No

Death Yes / No If yes cause of death

Time of death

12. Adverse effects

Adverse reaction noted:

Any other complication of gastric lavage/charcoal noted:

ANNEXURE IV

Modified Version of the Clinical Pulmonary Infection Score (CPIS)

Component	Value	Points
Temperature °C	≥36.5 and ≤38.4	0
	≥38.5 and ≤38.9	1
	≥39.0 and ≤36.0	2
Blood leukocytes per mm^3	≥4000 and ≤11000	0
	<4000 or >11 000	1
Tracheal secretions	Few	0
	Moderate	1
	Large	2
	Purulent	+1
Oxygenation Pao_2/Fio_2, mm Hg	>240 or presence of ARDS	0
	≤240 and presence of ARDS	2
Chest radiograph	No infiltrate	0
	Patchy or diffuse infiltrate	1
	Localized infiltrate	2

Namba's Grading Of Severity of OP Poisoning

MILD:

Nausea, vomiting, diarrhea, abdominal pain, Salivation, Wheezing.

MODERATE:

Weakness, Dysarthria, Fasciculation, Miosis, Bradycardia.

Severe:

Facial paralysis, Coma, Respiratory distress, pulmonary edema

APACHE II SCORE

The APACHE II score is a general measure of disease severity, based on current physiologic measurements, age and previous health condition. The score can help in the

assessment of patients to determine the level and degree of diagnostic and therapeutic intervention.

Components:

(1) acute physiology score (APS)

(2) age points

(3) chronic health points

Data collection:

- The data for the acute physiology is collected during the initial 24 hour period after ICU admission.

- The worst (most deranged) physiologic value is selected for grading.

Acute Physiology Score (APS)

Parameter	**Finding**	**Points**
rectal temp in C°	>= 41	+4
	39-40.9	+3
	38.5-38.9	+1
	36-38.4	0
	34-35.9	+1
	32-33.9	+2
	30-31.9	+3
	<= 29.9	+4
mean arterial pressure mm Hg	>= 160	+4
	130-159	+3
	110-129	+2
	70-109	0
	50-69	+2
	<= 49	+4
heart rate in beats/minute	>= 180	+4
	140-179	+3
	110-139	+2
	70-109	0
	55-69	+2
	40-54	+3
	<= 39	+4
respiratory rate in breaths/min	>=50	+4
	35-49	+3
	25-34	+1
	12-24	0
	10-11	+1
	6-9	+2
	<= 5	+4
oxygenation	A-aDO2 >= 500 and FIO2 >= 0.5	+4
	A-aDO2 350-499 and FIO2 >= 0.5	+3
	A-aDO2 200-349 and FIO2 >= 0.5	+2
	A-aDO2 < 200 and FIO2 >= 0.5	0
	PaO2 > 70 and FIO2 < 0.5	0
	PaO2 61-70 and FIO2 < 0.5	+1
	PaO2 55-60 and FIO2 < 0.5	+3
	PaO2 < 55 and FIO2 < 0.5	+4
arterial pH	>= 7.7	+4

	7.6-7.69	+3
	7.5-7.59	+1
	7.33-7.49	0
	7.25-7.32	+2
	7.15-7.24	+3
	< 7.15	+4
serum sodium	>= 180	+4
	160-179	+3
	155-159	+2
	150-154	+1
	130-149	0
	120-129	+2
	111-119	+3
	<= 110	+4
serum potassium	>= 7.0	+4
	6.0-6.9	+3
	5.5-5.9	+1
	3.5-5.4	0
	3.0-3.4	+1
	2.5-2.9	+2
	< 2.5	+4
serum creatinine in mg/dL	>= 3.5 and not acute renal failure	+4
	2.0-3.4 and not acute renal failure	+3
	1.5-1.9 and not acute renal failure	+2
	0.6-1.4 and not acute renal failure	0
	< 0.6 and not acute renal failure	+2
	>= 3.5 and acute renal failure	+8
	2.0-3.4 and acute renal failure	+6
	1.5-1.9 and acute renal failure	+4
	0.6-1.4 and acute renal failure	0
	< 0.6 and acute renal failure	+4
hematocrit in percent	>= 60	+4
	50-59.9	+2
	46-49.9	+1
	30-45.9	0
	20-29.9	+2
	< 20	+4
WBC count in thousands	>= 40	+4
	20-39.9	+2
	15-19.9	+1
	3-14.9	0
	1-2.9	+2
	< 1	+4
Glasgow Coma Score		15 - (Glasgow Coma Score)

where:

• The score for serum creatinine is doubled if the patient has acute renal failure.

• mean arterial pressure = ((systolic blood pressure) + (2 * (diastolic pressure))) / 3

If no blood gas data is available, then the serum bicarbonate can be used (I assume in place of the arterial pH):

Parameter	**Finding**	**Points**
serum bicarbonate in mmol/L	>= 52.0	+4
	41.0 − 51.9	+3
	32.0 − 40.9	+1

	22.0 − 31.9	0
	18.0 − 21.9	+2
	15.0 − 17.9	+3
	< 15.0	+4

Age Points

Age	Points
<= 44	0
45-54	2
55-64	3
65-74	5
>= 75	6

Chronic Health Points

Operative Status	Health Status	Points
nonoperative patient	history of severe organ insufficiency OR immunocompromised	5
	no history of severe organ insufficiency AND immunocompetent	0
emergency postoperative patient	history of severe organ insufficiency OR immunocompromised	5
	no history of severe organ insufficiency AND immunocompetent	0
elective postoperative patient	history of severe organ insufficiency OR immunocompromised	2
	no history of severe organ insufficiency AND immunocompetent	0

where:

• organ insufficiency or immunocompromised state must have preceded the current admission

• immunocompromised if: (1) receiving therapy reducing host defenses (immunosuppression, chemotherapy, radiation therapy, long term steroid use, high dose steroid therapy), or (2) has a disease severe enough to interfere with immune function such as malignant lymphoma, leukemia or AIDS

• liver insufficiency if: (1) biopsy proven cirrhosis, (2) portal hypertension, (3) episodes of upper GI bleeding due to portal hypertension, (4) prior episodes of hepatic failure, coma or encephalopathy

• cardiovascular insufficiency if: New York Heart Association Class IV

• respiratory insufficiency if: (1) severe exercise restriction due to chronic restrictive, obstructive or vascular disease, (2) documented chronic hypoxia, hypercapnia, secondary polycythemia, severe pulmonary hypertension, (3) respirator dependency

• renal insufficiency if: on chronic dialysis

APACHE II score =

= (acute physiology score) + (age points) + (chronic health points)

Interpretation:

• minimum score: 0

• maximum score: 71

• An increasing score is associated with an increasing risk of hospital death.

Knaus WA, Draper EA, et al. APACHE II: A severity of disease classification system. Critical Care Medicine. 1985; 13:818-829.

ANNEXURE V

Diagnostic Criteria for Sepsis

Infection,[a] documented or suspected, and some of the following:[b]

General variables

- Fever (core temperature >38.3°C)
- Hypothermia (core temperature <36°C)
- Heart rate >90 /min or >2 SD above the normal value for age
- Tachypnea
- Altered mental status
- Significant edema or positive fluid balance (>20 mL/kg over 24 hrs)
- Hyperglycemia (plasma glucose >120 mg/dL or 7.7 mmol/L) in the absence of diabetes

Inflammatory variables

- Leukocytosis (WBC count >12,000 /mm^3)
- Leukopenia (WBC count <4000 /mm^3)
- Normal WBC count with >10% immature forms
- Plasma C-reactive protein >2 SD above the normal value
- Plasma procalcitonin >2 SD above the normal value

Hemodynamic variables

- Arterial hypotension[b] (SBP <90 mm Hg, MAP <70, or an SBP decrease >40 mm Hg in adults or <2 SD below normal for age)
- SvO_2 >70%[b]
- Cardiac index (CI) >3.5 $L.min^{-1}.M^{-23}$

Organ dysfunction variables

- Arterial hypoxemia (PaO_2/FIO_2 <300)
- Acute oliguria (urine output <0.5 $mL.kg^{-1}.hr^{-1}$ or 45 mmol/L for at least 2 hrs)
- Creatinine increase >0.5 mg/dL
- Coagulation abnormalities (INR >1.5 or aPTT >60 secs)
- Ileus (absent bowel sounds)
- Thrombocytopenia (platelet count <100,000 /mm^3)
- Hyperbilirubinemia (plasma total bilirubin >4 mg/dL or 70 mmol/L)

Tissue perfusion variables

- Hyperlactatemia (>1 mmol/L)
- Decreased capillary refill or mottling

WBC, white blood cell; SBP, systolic blood pressure; MAP, mean arterial blood pressure; SvO_2, mixed venous oxygen saturation; INR, international normalized ratio; aPTT, activated partial thromboplastin time.

[a]Infection defined as a pathologic process induced by a microorganism;

[b]SvO2 sat >70% is normal in children (normally, 75–80%), and CI 3.5–5.5 is normal in children; therefore, NEITHER should be used as signs of sepsis in newborns or children;

[c]diagnostic criteria for sepsis in the pediatric population are signs and symptoms of inflammation plus infection with hyper- or hypothermia (rectal temperature >38.5 or < 35°C), tachycardia (may be absent in hypothermic patients), and at least one of the following indications of altered organ function: altered mental status, hypoxemia, increased serum lactate level, or bounding pulses.

Levy MM, Fink MP, Marshall JC, Abraham E, Angus D, Cook D, et al.International Sepsis Definitions Conference. Crit Care Med 2003;31:250-6.

Annexure vi

Method for Gastric lavage

The patient is placed in the left lateral decubitus position / head down position (20 tilt on the table). The length of tube to be inserted is measured and marked before insertion. A large bore 36–40 French or 30 English gauge tube (external diameter approximately 12–13.3 mm) should be used in adults; and 24–28 French gauge (diameter 7.8–9.3 mm) tube in children. The orogastric tube should be for single-use only. The lavage tube should have a rounded end and be sufficiently firm to be passed into the stomach via the mouth, yet flexible enough not to cause any mucosal damage. The tube should be lubricated with a hydroxyethylcellulose jelly.

Force should not be used to pass the tube, particularly if the patient is struggling. Once passed, the position of the tube should be checked either by air insufflation, while listening over the stomach, and/or by aspiration with pH testing of the aspirate. Traditionally, an aliquot of this sample has been retained for toxicological analysis though, except in the case of forensic examinations, the majority of laboratories now

prefer blood and urine for analysis. . Lavage is carried out using small aliquots of liquid. In an adult, 200–300 mL (preferably warm 38C) fluid, such as normal saline (0.9%) or water, should be used. In a child, warm normal saline (0.9%) 10 mL/kg body weight of should be given. The volume of lavage fluid returned should approximate the amount of fluid administered. Water should be avoided in young children because of the risk of inducing hyponatremia and water intoxication. Small volumes are used to minimize the risk of gastric contents entering the duodenum during lavage, since the amount of fluid affects the rate of gastric emptying (50). Warm fluids avoid the risk of hypothermia in the very young and very old and those

receiving large volumes of lavage fluid. Lavage should be continued until the recovered lavage solution is clear of particulate matter. It should be noted that a negative or poor lavage return does not rule out a significant ingestion.

Contraindications

- Loss of airway protective reflexes, such as in a patient with a depressed state of consciousness, unless intubated tracheally.
- Ingestion of a corrosive substance such as a strong acid or alkali.
- Ingestion of a hydrocarbon with high aspiration potential.
- . Patients who are at risk of hemorrhage or gastrointestinal perforation due to pathology, recent surgery, or other medical condition such as a coagulopathy.

Sno	NAME	HOSP.NO	R.NU	AGE	SEX	DM	HTN	SM	ALC	COPD	POI	T.ER	BP	HR	SAT	GCS	SOP	AC	IT	PIT	TIT	PLA	ENT	STP
1	Venkatesan S	839138c	2	23	1	2	2	2	1	2	1	160	140	120	99	15	1	1	1	1	1	1	1	1
2	Venkatesan	828021c	2	30	1	2	2	2	2	2	1	160	140	120	98	15	2	1	1	2	48	1	2	1
3	Jaganathan	862530c	2	63	1	2	2	1	1	2	4	30	150	92	98	9	N	1	1	1	0	1	1	2
4	Mani	856245c	1	50	1	2	2	1	1	2	4	200	110	110	65	7	N	1	1	1	0	1	2	1
5	Pitchandi	812060c	2	30	1	2	2	2	2	2	5	200	110	50	55	3	N	1	1	1	0	2	2	1
6	Govindaswamy	734772c	2	70	1	2	2	1	1	1	1	70	180	70	60	3	3	1	1	1	0	1	2	1
7	Sekar	850452c	1	25	1	2	2	1	1	2	1	120	120	80	96	15	3	1	1	2	7	1	2	1
8	Selvi	804265c	1	22	2	2	2	2	2	2	1	50	150	86	98	13	3	1	1	2	4	2	2	1
9	Latha	367563b	1	34	2	2	2	2	2	2	20	200	120	100	55	4	N	1	1	1	0	1	2	1
10	Deepalakshmi	832619c	1	21	2	2	2	2	2	2	20	220	110	80	92	8	N	1	1	1	0	2	2	1
11	Valarmathi	746597c	2	24	1	2	2	2	2	2	1	120	120	80	85	3	3	1	1	1	0	2	1	1
12	Eswaran	850182c	2	26	1	2	2	2	2	2	1	210	130	88	96	15	3	1	1	1	0	2	2	1
13	Venkatesan	846014c	1	30	1	2	2	2	1	2	1	30	110	126	80	7	3	1	1	1	0	2	2	1
14	Ramalingam	824766c	2	31	1	2	2	2	2	2	1	30	100	88	72	7	3	1	1	1	0	1	2	1
15	Balamurugan	745335c	1	21	1	2	2	2	2	2	1	105	110	80	96	4	3	1	1	1	0	2	1	1
16	Selvam	839091c	2	27	1	2	2	2	2	2	1	100	140	130	94	10	3	1	1	2	36	2	1	1
17	Sasikala	839240c	2	25	2	2	2	2	2	2	1	220	150	106	85	3	3	1	1	1	0	2	2	1
18	Gnanaprakasam	777440c	1	35	1	2	2	2	2	2	1	100	100	92	98	15	2	1	1	2	26	2	2	1
19	Shanmugham	852627c	1	23	1	2	2	2	2	2	1	200	130	80	94	15	3	1	1	2	48	1	1	1
20	Maran	747322c	2	23	1	2	2	2	2	2	1	210	100	140	96	15	1	1	1	1	15	2	1	1
21	Rajendiran	838502c	2	46	1	2	2	2	1	2	2	180	170	110	77	4	N	1	1	1	3	1	2	2
22	Sumitha	777503c	2	22	2	2	2	2	2	2	3	60	110	92	96	15	N	1	1	1	1	2	2	1
23	Mabu	824544c	1	23	2	2	2	2	2	2	4	140	90	92	98	15	N	1	2	N	N	1	2	1
24	Ponmathy	746156c	1	27	2	2	2	2	2	2	20	240	100	120	99	3	N	1	1	1	4	2	2	1
25	Rajeswari	742317b	2	24	2	2	2	2	2	2	20	70	110	116	99	7	N	1	1	1	3	2	1	1
26	Pappa Rao	812075c	1	29	1	2	2	2	2	2	1	110	120	60	96	14	2	1	2	N	N	1	2	1
27	Jhansi	789787c	2	18	2	2	2	2	2	2	1	240	90	150	97	12	3	1	2	N	N	1	2	1
28	Moorthy	240942b	2	34	1	2	2	2	2	2	1	60	110	90	99	15	1	1	2	N	N	1	2	1
29	Sunitha	815953c	1	14	2	2	2	2	2	2	1	30	130	118	99	15	1	1	2	N	N	1	1	1
30	Devaraj	863381c	1	42	1	2	2	2	2	2	1	150	130	124	96	15	2	1	2	N	N	1	1	1
31	Gunasekharan	758785c	1	30	1	2	2	2	1	2	1	200	150	110	99	15	1	1	2	N	N	1	1	1
32	Babu	746498c	2	25	1	2	2	2	2	2	1	240	130	100	99	15	1	1	2	N	N	1	2	1
33	Robinson	570640b	1	33	1	2	2	2	2	2	1	120	110	104	96	15	1	1	2	N	N	1	1	1
34	Jaikumar	850450c	1	19	1	2	2	2	2	2	1	200	110	96	90	15	3	1	2	N	N	1	1	1
35	Shanmugham	734423c	1	30	1	2	1	2	2	2	1	120	150	120	95	15	3	1	1	1	0	2	1	1
36	Srilatha	824529c	2	19	2	2	2	2	2	2	1	200	120	88	96	15	1	1	2	N	N	2	2	1
37	Marimuthu	812155c	2	30	2	2	2	1	1	2	1	240	100	100	96	15	1	1	2	N	N	1	1	1
38	Anushree	851691c	2	17	2	2	2	2	2	2	1	150	120	100	47	12	3	1	1	1	0	2	1	2
39	Bhanu	734289c	2	23	2	2	2	2	2	2	1	60	140	80	100	15	1	1	2	N	N	1	2	1
40	Eswaraiah	832616c	1	25	1	2	2	2	2	2	1	240	140	110	97	15	1	1	2	N	N	1	1	1
41	Ranganathan	871120c	1	40	2	2	2	2	2	2	1	45	110	84	98	15	1	1	2	N	N	1	1	1
42	Chandran	828099c	1	45	1	2	2	1	1	2	1	90	110	110	97	15	1	1	2	N	N	1	1	1
43	Mani	818727c	1	52	1	2	2	2	2	2	1	180	140	104	96	15	1	1	1	3	29	2	2	1
44	Vinila	812009c	1	20	2	2	2	2	2	2	1	210	130	130	96	15	1	1	2	N	N	1	1	1
45	Suresh	744809c	2	22	1	2	2	2	2	2	1	100	110	106	20	15	1	1	2	N	N	1	1	1
46	Anbazhagan	834195c	1	22	1	2	2	2	2	2	1	240	110	80	99	15	2	1	1	2	14	2	1	1
47	Sathya	734931c	1	18	1	2	2	2	2	2	1	210	110	110	96	12	3	1	1	1	0	2	1	1
48	Pachaiyappan	818898c	1	29	1	2	2	2	2	2	1	210	130	96	96	3	3	1	1	1	0	1	1	2
49	Shakthi	856053c	2	25	2	2	2	2	2	2	1	240	120	92	96	15	1	1	2	N	N	1	1	2
50	Sathya N	254171b	1	34	1	1	2	2	1	2	1	140	120	88	96	15	2	1	1	2	0	1	2	2
51	Chakravarthy	789284c	1	25	1	2	2	1	1	2	1	180	120	100	100	13	3	1	2	N	N	1	1	1
52	Ganesh	789624c	1	29	1	2	2	1	1	2	2	40	130	90	96	15	N	1	2	N	N	1	1	1

53	Pushpa	804055c	2	32	2	2	2	2	2	2	3	120	120	110	99	15	N	1	2	N	N	1	1	1
54	Hussaini Begum	870052c	1	18	2	2	2	2	2	2	3	120	120	80	96	15	N	1	2	N	N	1	1	2
55	Vinoth	876240c	1	21	1	2	2	2	2	2	4	180	80	60	96	14	N	1	2	N	N	1	2	1
56	Kumaran	804220c	1	23	1	2	2	2	2	2	4	120	120	90	96	15	N	1	2	N	N	1	1	1
57	Suresh	818577c	2	17	1	2	2	2	2	2	4	210	140	130	99	9	N	1	2	N	N	1	1	1
58	Radha	828045c	1	20	2	2	2	2	2	2	4	200	120	90	96	15	N	1	2	N	N	1	1	1
59	Indira	828044c	2	33	2	2	2	2	2	2	4	200	130	104	96	15	N	1	2	N	N	1	1	1
60	Ramesh	820146c	2	28	1	2	2	2	2	2	4	120	120	90	98	15	N	1	2	N	N	1	1	1
61	Thulasi	822101c	2	37	2	2	2	2	2	2	4	210	100	92	86	14	N	1	2	N	N	1	1	1
62	Jeyanthi	789483c	2	20	2	2	2	2	2	2	4	180	120	80	96	15	N	1	2	N	N	1	1	1
63	Munisekar	838183c	2	18	1	2	2	2	2	2	4	60	130	130	99	15	N	1	2	N	N	1	1	1
64	Jayashankar	846016c	1	23	1	2	2	2	2	2	4	50	130	110	100	15	N	1	2	N	N	1	1	1
65	Arul J	876245c	2	38	1	2	2	1	1	2	4	180	90	112	98	13	N	1	2	N	N	1	2	1
66	Ramamoorthy	733126c	2	65	1	2	2	1	2	2	5	200	110	70	99	15	N	1	2	N	N	1	1	1
67	Nagabhooshanam	804344c	1	35	1	2	2	2	2	2	5	240	170	68	96	15	N	1	2	N	N	1	1	1
68	Gopalakrishnan	850444c	2	23	1	2	2	2	2	2	5	210	140	106	96	15	N	1	2	N	N	1	1	1
69	Vijayalakshmi	804340c	2	36	2	2	2	2	2	2	6	190	100	100	96	15	N	1	2	N	N	1	1	1
70	Vinitha	838785c	2	14	2	2	2	2	2	2	6	180	110	100	99	15	N	1	2	N	N	1	1	2
71	Janaki	863248c	2	60	2	1	2	2	2	2	6	210	130	104	99	15	N	1	2	N	N	1	1	1
72	Birunda	824702c	2	25	2	2	2	2	2	2	6	220	100	96	96	15	N	1	2	N	N	1	1	1
73	Kalpana	529238c	1	25	2	2	2	2	2	2	7	150	130	90	100	12	N	1	2	N	N	1	1	1
74	Susila	592512b	1	37	2	2	1	2	2	2	7	60	160	68	99	14	N	1	1	1	2	2	2	1
75	Prakasam	789538c	1	34	1	2	2	2	1	2	8	215	130	100	98	15	N	1	2	N	N	1	2	1
76	Poornima	686631b	2	15	2	2	2	2	2	2	8	90	100	80	97	14	N	1	2	N	N	2	2	1
77	Ranganathan	832618c	1	53	1	2	2	2	2	2	9	120	130	72	98	11	N	1	2	N	N	1	1	1
78	Ranganathan	832618c	2	53	1	2	2	2	2	2	9	180	130	80	90	11	3	1	2	N	N	1	1	1
79	Kalavathy	794949c	2	37	2	2	2	2	2	1	10	240	120	80	99	15	N	1	2	N	N	1	1	1
80	Sathya	826271c	2	19	2	2	2	2	2	2	11	220	120	88	96	15	N	1	2	N	N	1	1	1
81	Nirmala	714567c	1	36	2	2	1	2	2	2	13	210	135	110	96	15	N	1	2	N	N	1	1	2
82	Rashida	513306b	2	25	2	2	2	2	2	2	13	210	140	100	96	15	N	1	2	N	N	1	1	1
83	Radhammal	395019b	2	70	2	2	2	2	2	2	14	180	130	80	96	15	N	1	2	N	N	1	1	1
84	Vijay	665268a	2	18	1	2	2	1	2	2	15	60	110	110	100	14	N	1	2	N	N	1	1	1
85	Kishore K	777458c	1	25	1	2	2	1	1	2	15	120	120	120	96	15	N	1	2	N	N	1	1	1
86	Nathiya	834939c	1	17	2	2	2	2	2	2	15	60	110	90	96	15	N	1	2	N	N	1	1	1
87	Alamelu	846488c	1	26	2	2	2	2	2	2	15	210	110	100	99	15	N	1	2	N	N	1	1	1
88	Subashini	789399c	2	38	2	2	2	2	2	2	16	120	100	130	97	15	N	1	2	N	N	1	1	1
89	Janani	714448c	1	17	2	2	2	2	2	2	17	120	120	96	96	15	N	1	2	N	N	1	1	1
90	Vasu	523272b	2	34	1	2	2	2	2	2	17	120	120	96	96	15	N	1	2	N	N	1	1	1
91	Chithra	734334c	2	29	2	2	2	2	2	2	17	70	120	92	98	15	N	1	2	N	N	1	1	1
92	Prabhu	780485c	1	39	1	1	2	1	1	2	17	180	110	100	97	15	N	1	2	N	N	1	1	1
93	Saravanan	411109c	1	18	1	2	2	1	1	2	17	220	110	108	98	15	N	1	2	N	N	1	1	1
94	Sengamalar	863408c	1	37	2	2	2	2	2	2	17	210	160	102	99	15	N	1	2	N	N	1	1	1
95	Sudhakar	812008c	2	26	1	2	2	2	2	2	17	210	130	92	99	15	N	1	2	N	N	1	2	1
96	Thirumoorthy	823013c	1	25	1	2	2	2	1	2	17	135	110	85	96	15	N	1	2	N	N	1	1	1
97	Dhanabackiam	863412c	2	70	2	1	2	2	2	2	17	180	180	120	96	15	N	1	2	N	N	1	1	1
98	Shankar	289427c	1	33	1	2	2	1	1	2	18	120	120	90	96	15	N	1	2	N	N	1	1	1
99	Dinesh	789956c	1	25	1	2	2	2	2	2	18	60	140	120	88	9	N	1	2	N	N	1	1	1
100	Srinivasulu	839330c	2	16	1	2	2	2	2	2	18	210	110	100	97	15	N	1	2	N	N	1	1	1
101	Rajesh	824798c	2	22	2	2	2	1	1	2	18	220	100	110	95	15	N	1	2	N	N	1	2	1
102	Jayakumari	141617a	1	24	2	2	2	2	2	2	19	120	110	88	96	15	N	1	2	N	N	1	1	1
103	Moorthy	850013c	1	40	1	2	2	1	1	2	20	210	110	124	94	15	N	1	2	N	N	1	1	1
104	Anitha	876241c	1	17	2	2	2	2	2	2	4	160	140	100	96	15	N	1	2	N	N	1	1	1

RIT	IM	APAC	TR	DMV	DICU	D.HS	DIE	DIAL	PCM	HB	CREAT	TC	RBS	NA	K	BIC	LD	PCHOL	POUT	TPN	TRE	TITPN	SEP
2	2	8	2	5	N	5	1	2	2	14.8	1.2	11000	131	144	3.1	18	2	317	1	2	N	2	1
2	1	5	2	7	N	9	1	2	2	16.0	.8	15100	131	145	3.2	22	2	1460	2	N	N	N	1
2	N	15	2	3	N	3	1	2	2	19.7	1.1	13900	120	138	4.2	18	2	N	1	1	N	1	1
2	N	18	2	4	N	4	1	2	2	14.5	1.4	8600	128	143	3.8	16	2	N	1	1	N	1	1
2	N	23	2	3	3	3	1	1	1	13.7	4.7	15000	112	146	2.4	12	1	N	1	1	N	1	1
2	2	20	2	2	N	16	2	2	2	13.2	1.1	5200	80	141	4.0	16	2	1237	1	2	7	2	2
2	2	7	2	1	N	1	1	2	2	5.6	.7	17400	126	136	3.5	19	2	254	2	N	N	N	2
2	1	6	1	13	6	13	1	2	2	13.8	.8	13300	231	141	2.6	22	2	476	2	N	N	N	2
1	N	20	2	2	N	2	1	2	2	11.4	.7	8600	106	138	3.9	21	2	N	2	N	N	N	2
2	N	14	2	5	4	5	1	2	2	12.1	.8	15300	138	140	3.1	19	2	N	2	N	N	N	2
2	1	20	1	10	8	14	2	2	2	10.6	.8	13300	86	146	4.6	18	2	190	1	4	9	4	2
2	2	12	1	15	17	22	2	2	2	14.8	1.5	17700	287	137	3.0	19	2	317	1	3	14	3	1
2	1	9	1	14	16	23	2	2	2	19.3	1.0	21500	104	146	3.7	19	2	476	1	6	18	6	2
2	2	18	2	2	N	16	2	2	2	16.0	1.4	13800	144	148	3.1	16	2	381	1	2	10	2	2
2	2	18	1	12	14	20	2	2	2	16.5	.9	16400	108	136	4.0	17	2	508	2	N	N	N	2
1	1	16	1	20	21	24	2	2	2	17.9	1.2	15400	132	144	3.2	18	2	635	1	2	12	2	2
1	1	22	1	9	10	22	2	2	2	13.4	.9	14400	191	144	2.8	18	2	698	2	N	N	N	2
2	1	10	1	8	9	24	2	2	2	18.2	.8	17600	128	144	3.4	21	2	698	2	N	N	N	2
2	1	3	2	9	N	13	2	2	1	13.9	1.3	25100	134	145	3.3	24	2	825	2	N	N	N	2
2	1	7	2	8	6	10	1	2	2	15.4	1.0	13000	132	140	4.2	25	2	444	1	3	N	3	1
2	N	25	2	1	N	4	2	2	2	17.6	.9	11000	171	139	2.7	17	2	1237	2	N	N	N	2
1	N	8	2	7	9	12	2	2	2	10.2	1.0	25500	132	146	4.3	15	1	N	2	N	N	N	1
N	N	4	2	N	N	15	2	2	2	13.4	1.4	19700	97	139	3.2	22	1	N	2	N	N	N	2
2	N	20	2	9	11	12	2	1	2	12.4	.8	5900	193	138	3.5	19	2	N	1	1	12	1	1
1	N	9	2	7	7	12	2	2	2	11.7	.7	9500	109	133	3.7	24	2	N	2	N	N	N	2
N	2	4	2	N	N	4	2	2	2	13.6	1.0	11200	117	139	4.7	21	2	381	2	N	N	N	2
N	2	12	2	N	N	4	2	2	2	12.3	1.0	17200	171	136	3.5	18	2	190	2	N	N	N	2
N	2	9	2	N	N	6	2	2	2	15.8	.7	11500	150	142	3.4	20	2	253	2	N	N	N	2
N	2	9	2	N	N	5	2	2	2	10.1	.7	9600	85	143	3.1	19	2	254	2	N	N	N	2
N	2	2	2	N	N	5	2	2	2	14.2	.9	10900	143	135	4.1	22	2	254	2	N	N	N	2
N	2	6	2	N	N	6	2	2	2	17.0	.9	9400	89	141	3.9	21	2	286	2	N	N	N	2
N	2	5	2	N	N	5	2	2	2	19.0	1.2	18100	119	144	4.4	22	2	317	2	N	N	N	2
N	2	6	2	N	N	4	2	2	2	14.5	1.0	11600	168	144	3.0	21	2	317	2	N	N	N	2
N	2	5	2	N	N	7	2	2	2	13.8	.8	8100	106	141	3.3	14	2	317	2	N	N	N	2
2	2	8	2	2	8	17	2	2	2	16.2	1.2	17200	170	136	2.9	19	2	317	2	N	N	N	2
N	2	6	2	N	1	6	2	2	2	13.2	.6	21100	110	140	3.7	20	2	349	2	N	N	N	2
N	2	5	2	N	N	4	2	2	2	15.1	1.6	13600	106	148	3.0	22	2	381	2	N	N	N	2
2	2	22	2	4	3	6	2	2	2	13.3	.8	9800	140	140	2.6	17	2	412	2	N	N	N	2
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N	2	5	2	N	N	4	2	2	2	16.9	1.0	14000	98	138	3.7	22	2	539	2	N	N	N	2
N	2	7	2	N	N	4	2	2	2	17.4	.8	16500	108	136	3.1	21	2	571	2	N	N	N	2
N	2	6	2	N	N	4	2	2	2	16.1	.9	16900	104	146	3.4	23	2	635	2	N	N	N	2
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N	2	8	2	N	N	4	2	2	2	16.9	1.1	10900	90	136	4.1	20	2	984	2	N	N	N	2
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2	2	16	2	2	N	2	2	2	2	16.8	1.0	8200	102	133	4.0	21	2	3459	2	N	N	N	2
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2	2	3	2	3	N	5	2	2	2	13.8	.6	13800	208	144	4.1	18	2	5394	2	N	N	N	2
N	2	8	2	N	N	4	2	2	2	15.6	.7	9100	85	141	3.5	20	2	6124	2	N	N	N	2
N	N	16	2	N	N	4	2	2	2	17.6	1.2	9800	184	145	3.2	14	2	4664	2	N	N	N	2

N	N	7	2	N	N	3	2	2	2	15.0	.7	10200	120	142	3.8	19	2	N	2	N	N	N	2
N	N	4	2	N	N	2	2	2	2	13.4	.7	12800	106	138	3.4	16	2	N	2	N	N	N	2
N	N	8	2	N	N	3	2	2	2	15.2	.8	8200	81	136	2.4	21	2	N	2	N	N	N	2
N	N	4	2	N	N	2	2	2	2	17.1	.8	9600	110	135	3.9	27	2	N	2	N	N	N	2
N	N	12	2	N	N	3	2	2	2	13.5	.8	15300	140	138	4.1	21	2	N	2	N	N	N	2
N	N	7	2	N	N	2	2	2	2	10.5	.7	12900	132	141	3.3	17	2	N	2	N	N	N	2
N	N	4	2	N	N	2	2	2	2	14.1	.9	8800	140	138	3.5	19	2	N	2	N	N	N	2
N	N	7	2	N	N	2	2	2	2	14.9	1.2	10100	108	143	3.4	18	2	N	2	N	N	N	2
N	N	8	2	N	N	2	2	2	2	10.3	.8	17900	102	136	3.2	19	2	N	2	N	N	N	2
N	N	4	2	N	N	2	2	2	2	9.4	.7	10100	104	135	4.3	21	2	N	2	N	N	N	2
N	N	9	2	N	N	2	2	2	2	16.4	.8	8800	148	144	3.1	21	2	N	2	N	N	N	2
N	N	7	2	N	N	3	2	2	2	16.2	1.0	16900	100	148	3.3	21	2	N	2	N	N	N	2
N	N	4	2	N	N	3	2	2	2	13.2	1.4	10500	201	138	3.8	22	2	N	2	N	N	N	2
N	N	8	2	N	N	8	2	2	1	12.4	1.2	20200	194	138	3.6	15	2	N	2	N	N	N	2
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N	N	7	2	N	N	7	2	2	1	15.2	.8	32500	142	136	4.5	20	2	N	2	N	N	N	2
N	N	5	2	N	N	4	2	2	2	14.9	.7	9400	104	146	3.0	23	2	N	2	N	N	N	2
N	N	3	2	N	N	7	2	2	1	13.2	.7	7800	98	143	3.5	23	2	N	2	N	N	N	2
N	N	8	2	N	N	4	2	2	1	11.5	.8	8400	114	135	4.4	21	2	N	2	N	N	N	2
N	N	5	2	N	N	5	2	2	1	9.3	.7	11600	148	133	3.1	17	2	N	2	N	N	N	2
N	N	4	2	N	N	2	2	2	2	12.2	.7	10200	108	136	4.0	16	2	N	2	N	N	N	2
2	N	5	2	3	5	8	2	2	1	13.5	.8	11600	88	143	4.0	20	2	N	2	N	N	N	2
1	N	3	2	N	N	3	2	2	2	11.9	.6	6100	89	130	4.0	22	2	N	2	N	N	N	2
N	N	10	2	N	1	3	2	1	2	12.6	.7	9800	80	134	3.1	10	2	N	2	N	N	N	2
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N	N	4	2	N	N	5	2	2	2	14.1	.8	9100	127	135	3.9	20	2	N	2	N	N	N	2
N	N	0	2	1	N	4	2	2	2	13.2	.8	3700	106	140	4.0	26	2	N	2	N	N	N	2
N	N	4	2	N	N	5	2	2	2	12.3	.8	8100	62	147	4.3	26	2	N	2	N	N	N	2
N	N	3	2	N	N	2	2	2	2	14.9	.7	14300	100	143	3.7	22	2	N	2	N	N	N	2
N	N	12	2	N	N	2	2	2	2	11.2	.7	5900	178	134	3.4	18	2	N	2	N	N	N	2
N	N	7	2	N	N	2	2	2	2	14.1	.8	9000	112	143	3.4	21	2	N	2	N	N	N	2
N	N	7	2	N	N	2	2	2	2	15.7	.9	13600	79	139	4.2	16	2	N	2	N	N	N	2
N	N	8	2	N	N	2	2	2	2	13.6	.7	8400	132	143	3.2	19	2	N	2	N	N	N	2
N	N	4	2	N	N	2	2	2	2	12.1	.6	5600	91	139	3.0	21	2	N	2	N	N	N	2
N	N	12	2	N	N	3	2	2	2	12.9	.9	19500	104	139	4.0	15	2	N	2	N	N	N	2
N	N	5	2	N	N	2	2	2	2	10.9	.6	12500	102	135	4.5	21	2	N	2	N	N	N	2
N	N	4	2	N	N	2	2	2	2	13.5	.9	7900	104	145	3.9	24	2	N	2	N	N	N	2
N	N	4	2	N	N	2	2	2	2	13.2	.8	8800	108	141	4.4	23	2	N	2	N	N	N	2
N	2	4	2	N	N	3	2	2	2	16.1	1.3	10800	251	139	3.7	24	2	N	2	N	N	N	2
N	N	7	2	N	N	2	2	2	2	14.2	.9	7800	101	143	3.1	20	2	N	2	N	N	N	2
N	N	5	2	N	N	2	2	2	2	15.2	.6	16200	101	139	3.4	20	2	N	2	N	N	N	2
N	N	5	2	N	N	3	2	2	2	16.0	1.0	14400	118	141	3.4	17	2	N	2	N	N	N	2
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N	N	18	2	N	N	2	2	2	2	16.1	1.1	12600	211	141	3.2	18	2	N	2	N	N	N	2
N	N	5	2	N	N	2	2	2	2	14.9	.9	15300	112	147	3.2	23	2	N	2	N	N	N	2
N	N	3	2	N	N	5	2	2	2	14.6	.9	10600	113	144	2.9	24	2	N	2	N	N	N	2
N	N	3	2	N	N	2	2	2	2	11.0	.8	13100	156	139	3.0	19	2	N	2	N	N	N	2
N	N	10	2	N	N	2	2	2	2	16.3	1.0	17800	137	140	3.2	22	2	3459	2	N	N	N	2
N	N	3	2	N	N	3	2	2	2	15.4	.7	9800	85	140	4.0	18	2	N	2	N	N	N	2